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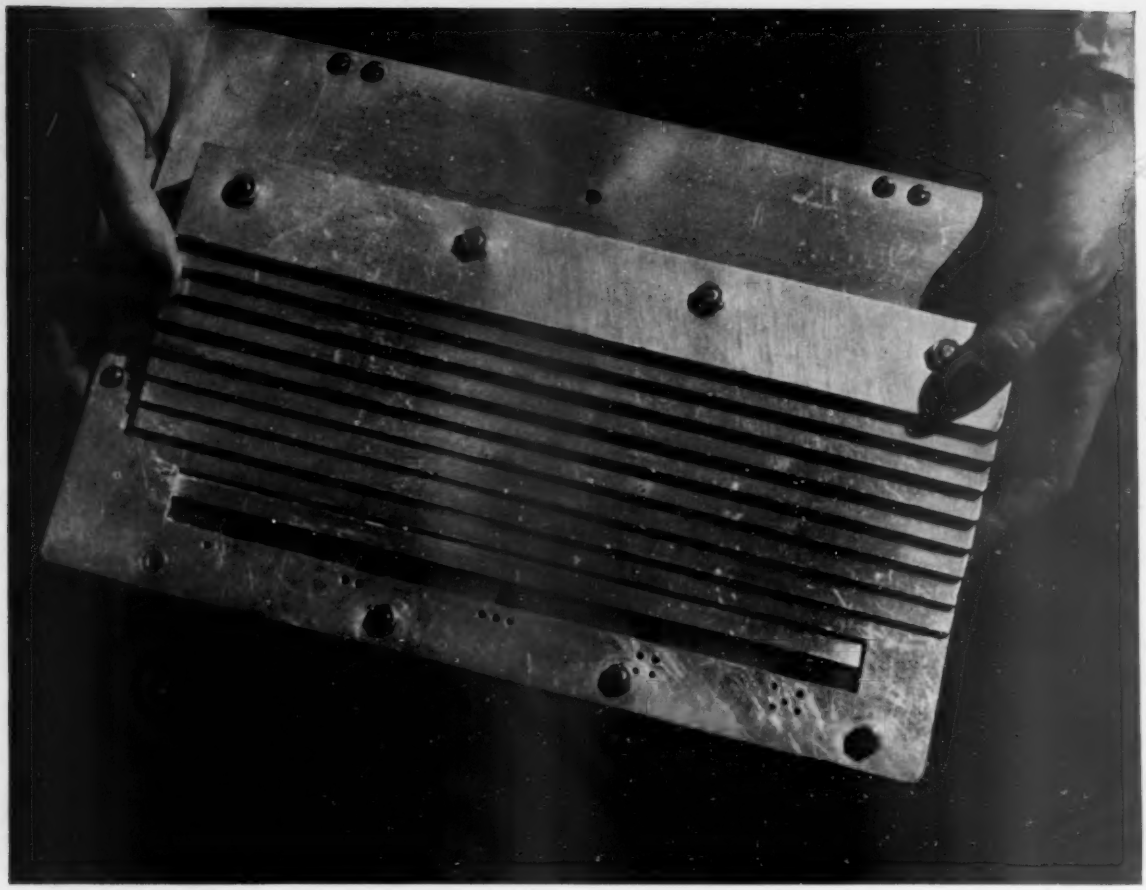

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

VOL. 50 AUGUST, 1943 NO. 2

THE CONTROL OF DIAGNOSTIC QUALITY IN ROENTGENOGRAMS OF THE CHEST*

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I. INTRODUCTION

THERE can be little question that roentgenography is of greatest clinical value only when the radiologist is provided with roentgenograms of consistently high quality. This is true regardless of the anatomical structure under consideration, but is particularly so in roentgenography of the chest. If diagnostically excellent roentgenograms are to be produced routinely, adequate control of the various factors which determine roentgenographic quality must be maintained at all times. It is unfortunate that in the past such control has been difficult to achieve; however, this situation is rapidly changing and it is hoped that before long new methods will effectively overcome many of the difficulties that heretofore have existed.

Before pursuing a discussion of the various problems relating to the control of roentgenographic quality, we should pause long enough to establish clearly in our minds the criteria which determine the diagnostic value of a roentgenogram. From this it will be possible to appreciate more fully the many factors which influence roentgenographic quality and to understand more completely the measures which may be applied to effect their control.

The images of the various anatomical structures recorded in a roentgenogram may be perceived only because the density† of each image is greater or less than those of the surrounding tissues. Furthermore

† The term, density, refers to the blackening of a film. Numerically, it is equal to the logarithm of the reciprocal of the light transmission of the film; that is,

$$D = \text{Log}\,\frac{1}{T}. \qquad \text{(a)}$$

Thus, a film which transmits one-tenth of the light incident upon it has a density of 1.0 (i.e.

$$D = \text{Log}\,\frac{1}{1/10} = \text{Log}\,10 = 1.0).$$

This method of expressing density is an extremely logical one. To illustrate this, let us imagine that we have two roentgenograms, each of which has a density of 1.0. When the roentgenograms are superimposed upon one another and a light projected through them, the light is reduced to one-tenth of its original intensity on passing through the first film, and to one-tenth of one-tenth (or to one one-hundredth) of its original intensity after it has passed through the second film. According to equation (1) the density of the two roentgenograms taken together then is 2.0 or the same value that would be obtained if the densities of the individual roentgenograms were merely added together. Thus, a density of 2.0 actually means that there is twice as much effective light-absorbing material present as when the density is 1.0. Or, in more general terms, the density, as determined by equation (1), is a direct measure of the effective quantity of light-absorbing material present in a roentgenogram. (Two films of the same density do not necessarily contain the same absolute quantities of silver. Density, therefore, is not a reliable index of the quantity of silver in a film.)

Many roentgenologists are not accustomed to thinking of film-blackening in terms of density. It may be worth while to point out, therefore, that the densities of the hilar images of the roentgenogram reproduced in Figure 1 have values approximating 0.4; the densities of the darkest portions of the peripheral lung fields range almost to 1.5.

* Presented before the Forty-third Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 15–18, 1942.

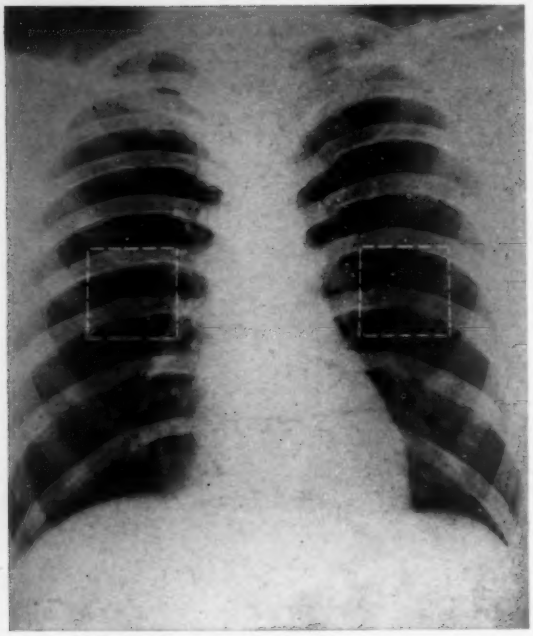

Fig. 1. Roentgenogram of the chest illustrating portions of lung fields scanned by exposure meter's radiation detector.

the greater that these differences in density become, the more easily the images may be distinguished. For example, in a roentgenogram of the chest, it is extremely easy to identify the images of the ribs where they pass across the dense background of the lung fields, but relatively difficult to detect them where they are superimposed upon the almost equally dense images of the soft tissues below the diaphragm and in the lateral chest walls. It is customary to speak of the differences in density of adjacent roentgenographic images as contrast. From the foregoing it is clear that contrast plays a major rôle in determining the ease with which a roentgenogram may be interpreted; indeed, it constitutes one of the principal criteria which determine the diagnostic value of a roengenogram.

The various factors which influence the contrast exhibited in roentgenograms of the chest may be divided into two general categories: (*a*) those which affect the characteristics of the roentgen-ray beam falling on the film (e.g., the kilovoltage applied to the roentgen tube, the anatomical properties of the particular chest under examination, and the presence or absence of a Potter-Bucky grid), and (*b*) those which affect the characteristics of the roentgenographic film itself (e.g., the exposure received by the film and the process of developing).

Contrary to general belief, the kilovoltage applied to the roentgen tube usually has a relatively small effect on contrast. During the past year we have made a comprehensive quantitative study of the various factors which influence the roentgenographic contrast of bone, fibrillar and fat tissues and find that in chests less than 20 cm. in thickness the contrast of lung tissue may be expected to increase less than 40 per cent when the kilovoltage is decreased from 90 to 55 kv. (peak). Such a change is usually difficult to perceive and must be considered unimportant. In passing it may be worth while to point out that the ribs in films exposed with low kilovoltage are frequently under-penetrated and the superimposed lung fields obscured. To prevent this occurrence kilovoltages in excess of 60 kv. (peak) should be employed. In chests greater than 25 cm. in thickness the contrast of lung tissues may be expected to increase in excess of 60 per cent when the kilovoltage is decreased from 90 to 55 kv. (peak). This change is sufficiently great to be clearly perceptible and an improvement in roentgenographic quality often may be obtained by exposing these exceptionally heavy chests at a relatively low kilovoltage. However, restrictions imposed by the capacity of the roentgenographic equipment at hand do not usually permit the use of potentials below 70 kv. (peak).

The anatomical properties of the chest have a decided influence on roentgenographic contrast. To illustrate this it need only be recalled that parenchymal lesions may be identified more easily in thin than in obese individuals.

The Potter-Bucky grid by virtue of its ability to prevent scattered radiation from

reaching the film increases contrast from two to three times, depending on the thickness of the chest under examination and to a less extent on the kilovoltage applied to the roentgen tube.

The exposure received by a roentgenogram influences contrast through its effect upon film density. The characteristics of present-day brands of film are such that the contrast of images whose densities fall below 0.3 is inherently low. Such images appear flat, poorly defined, and yield little diagnostic information. The images whose densities lie between 0.3 and 2.5, on the other hand, have a relatively high degree of contrast and exhibit maximum definition. When the density of 2.5 is exceeded image contrast again diminishes. The relation between contrast and density in a typical roentgenographic film, exposed with intensifying screens, is shown in Figure 2.

Although contrast is greatest when the densities of a film have values falling between 0.3 and 2.5 this entire range is not useful roentgenographically for when roentgenograms are viewed in the usual way in a uniformly lighted viewbox, the eye fails to perceive gradations in film blackening when the densities lie above 1.5. Accordingly, if maximum effective contrast is to be obtained, the exposure received by a film must be such that the densities of the significant areas fall between 0.3 and 1.5.

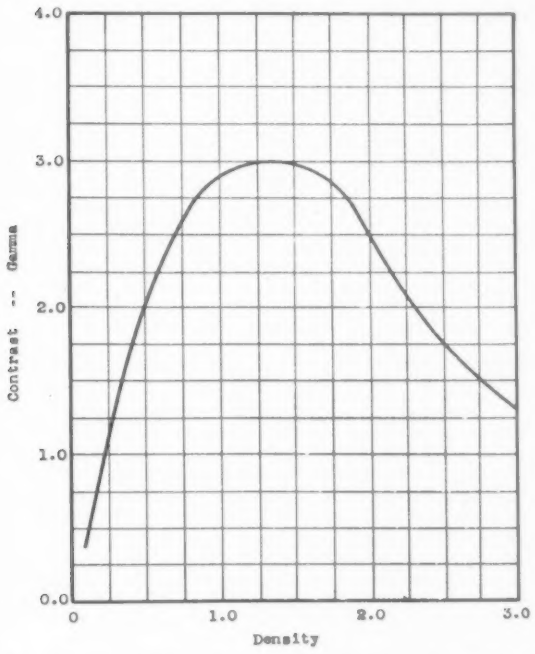

Fig. 2. The relation between contrast and density in a typical roentgenogram.

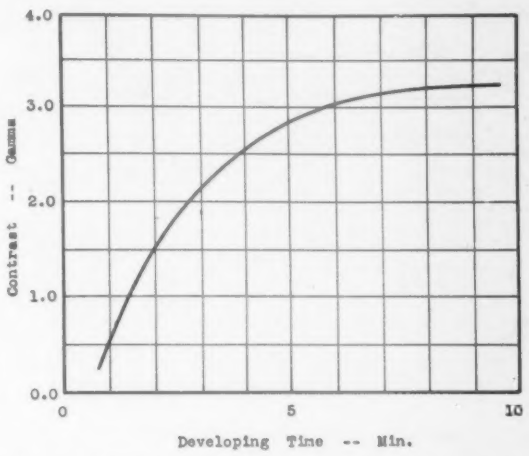

Fig. 3. The relation between contrast and developing time in a typical roentgenogram.

The process of developing is an important factor, determining contrast. In general, contrast increases as the process of developing progresses and approaches a maximum when the developing time recommended by the manufacturer of the film is reached. The relation between developing time and contrast for Eastman blue brand film exposed with intensifying screens and developed in a pictol-hydroquinone developer at 65°F. (recommended developing time, 5 minutes) is shown in Figure 3.

Since the structural detail exhibited in a roentgenogram improves when contrast increases, it may be reasonably assumed that roentgenograms of maximum diagnostic quality will be obtained only when all of the factors which enhance contrast are utilized. This, however, is not always true for many of the factors which usually increase contrast may, under special circumstances, cause a diminution in contrast. The explanation of this paradoxical

situation may be found in the fact that when contrast increases, the density-range occupied by the significant images of a film also becomes greater. Accordingly when contrast exceeds a certain level, some of the significant densities will fall outside the useful range of film blackening. Since such densities from a diagnostic

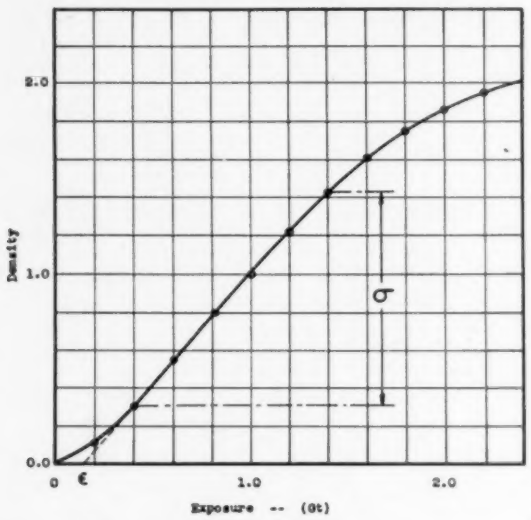

Fig. 4. The relation between the exposure received by a film and the resulting density or degree of blackening.

standpoint are of little value, it is evident that contrast should not be increased beyond that point at which the densities of the significant images of a roentgenogram occupy the entire useful range of film blackening.

The following is an excellent example of excessive contrast in chest roentgenography: Densitometric examinations in this laboratory reveal that in an average chest roentgenogram about two-thirds of the useful range of fim blackening is occupied by significant densities when the roentgenogram has been made with correct exposure, without a grid and with optimum development. The contrast and detail in some portions of such a roentgenogram might be improved by the use of a grid. Since, however, the density-range of the film would be increased very considerably by this procedure, many of the significant densities then would have values less than 0.3 and greater than 1.5; as a result the overall quality of the roentgenogram would be appreciably reduced. It is therefore unwise to use routinely the vertical reset grid in chest roentgenography even though it increases contrast to a marked degree.

It would be unfair not to mention here the special instances in which a grid is extremely useful. Not infrequently the images of pathological processes provide little detail of their internal structure. This often may be traced to the presence of scattered radiation fogging the film. If such is the case, the use of a grid will do much to improve roentgenographic quality.

It frequently is advantageous to employ a grid when heavy subjects are examined. When a grid is not used in these cases the significant densities in the resulting roentgenograms tend to occupy a relatively small portion of the useful range of film blackening. Under such circumstances, none of these densities may be expected to fall below 0.3 or above 1.5 when a grid is used, and the added contrast so obtained is obviously valuable.

A grid is also useful in photoroentgenography where films are exposed on one side only. The contrast of such roentgenograms is inherently lower than that of films exposed with front and back intensifying screens and a grid serves as an extremely useful tool in compensating for this effect.

In the foregoing paragraphs, the various factors which influence roentgenographic quality have been reviewed. It has been shown that optimum diagnostic quality may be expected in chest roentgenograms only when the following criteria* are ful-

* It may seem a little paradoxical to the reader to find that the criteria which determine roentgenographic quality seem to leave little room for argument on the subject of what constitutes a diagnostically excellent roentgenogram of the chest when it is well known that there exists among roentgenologists a wide difference of opinion on the matter. For example, in a survey made by Weyl and Warren[11] a few years ago in which chest roentgenograms from many parts of the country were obtained, the appearances of the roentgenograms varied between almost unbelievably wide limits. Does this mean that there are many roentgenologists who unknowingly are placing themselves at a disadvantage by not providing themselves with chest roentgeno-

filled: (1) Roentgenographic exposure must be such that the densities of the significant areas of a film fall within the limits of 0.3 and 1.5. (2) The kilovoltage applied to the roentgen tube is not critical but an intermediate kilovoltage (e.g. 70 kv. (peak)) is probably optimum in most cases. (3) A Potter-Bucky grid should be used only under special circumstances; it should not be used routinely. (4) Films must undergo standard development.

An examination of these prerequisites reveals that the production of diagnostically excellent roentgenograms of the chest is primarily dependent upon adequate control of roentgenographic exposure and of the process of developing.

II. CONTROL OF ROENTGENOGRAPHIC EXPOSURE

We have seen that the densities of the significant areas of chest roentgenograms must have values falling between the limits of 0.3 and 1.5 if optimum diagnostic quality is to be obtained. This obviously will occur with greatest certainty if the average densities of the films are maintained at levels midway in the useful range of film blackening (i.e. have values approximating a density of 0.9).

In some instances, some variation from this value may occur without loss of quality, the amount of variation that may be permitted in a particular case depending on the density-range occupied by the diagnostic portions of the film. For example in a roentgenogram in which the lightest significant area has a density of 0.7 and the darkest area a density of 1.1, the densities may increase or decrease 0.4 unit before any lie outside the useful range of film blackening. On the other hand, any variation in a film in which the lightest density is 0.3 and the darkest density is 1.5 will cause a reduction in diagnostic quality. In average chest roentgenograms, the lighter areas (hilar regions) have densities of approximately 0.5, whereas the densities of the darker regions (peripheral lung fields) approximate 1.3. Therefore the average density of an average chest roentgenogram may vary 0.2 unit in either direction of the optimum density of 0.9 without loss in quality. Since in practice one frequently encounters roentgenograms in which the density range occupied by the significant images is greater than average it may be reasonably stated that adequate control of roentgenographic exposure requires that the average density of chest roentgenograms vary not more than ± 0.1 unit of a density of 0.9.

The exposure* required to produce a

grams of optimum quality or does it mean that the criteria, outlined above, are unnecessarily rigid? The answer to this question is not as difficult as it might at first seem. In the above discussion reference has been repeatedly made to the term, "the significant areas of a roentgenogram." Now what constitutes the significant areas of a chest roentgenogram? Do they merely include the lung fields and hilar areas or do they also include the entire tracheal region and even the thoracic spine? In this institution we prefer to include only the former areas but there are many roentgenologists who wish to visualize in some detail the vertebral column. It is this difference of opinion upon which the observations of Weyl and Warren may be explained, for it is obvious that a roentgenogram in which the significant portions are considered to include only the lung fields and hilar areas will be considerably lighter than a roentgenogram which also visualizes portions of the thoracic spine.

It would be desirable, of course, if roentgenologists could come to some agreement on the matter of what constitutes the significant areas of a chest roentgenogram. We can see no possibility of this occurring, however, since the opinions of the individual roentgenologist have become so well established that they are not likely to change. In passing, however, we would like to point out that to consider the lung fields and hilar areas alone as significant is a rather sound policy. As we have seen, the densities of these regions in the average chest roentgenogram occupy about 70 per cent of the useful range of film blackening. When the trachea and portions of the thoracic spine are also considered significant the diagnostic densities frequently spread beyond the useful density-range. This is particularly undesirable because the lung fields being the darkest portions of the roentgenogram suffer the greatest loss of definition under such circumstances. It seems wiser to obtain routinely the best possible roentgenograms of the lung fields and hilar areas and then, if pathologic change in other structures is suspected, to re-examine the patient with special reference to these regions.

* Within the useful range of film blackening the density of a uniformly exposed and processed roentgenogram is closely proportional to the exposure received by the film. This relationship is shown graphically in Figure 4 and may be expressed by the equation,

$$D=\sigma(E-\epsilon) \qquad \text{(b)}$$

where D is the density of the film, E is the exposure received by the film, σ is a constant whose value is dependent on the film's sensitivity, and ϵ is a constant. The term, exposure, as used in equation (b) is defined as the product of the effective intensity, G, of the radiation impinging on the film (photographic flux density) by the exposure time, t; therefore,

$$D=\sigma(Gt-\epsilon) \qquad \text{(c)}$$

Equation (c) specifies the conditions for a uniformly blackened film. Since the relationship between density and exposure is

particular film density is a constant when a particular brand of film is employed. The term, exposure, as herein used, is employed in its strictly physical sense and is defined as the product of the effective intensity of the radiation falling upon the film by the exposure time. It will be clearly evident then that the equation,

$$\bar{G} \times t = a_{0.9} \tag{1}$$

where G is the average effective intensity of the radiation falling on the film, t is the exposure time, and $a_{0.9}$ is a constant representing the exposure required to produce a film density of 0.9, specifies the conditions for correct exposure. This equation indicates that if the intensity of the radiation impinging on a film is high (e.g. thin-chested individuals) the exposure time must be short; conversely, if the intensity is low (thick-chested individuals) the exposure time must be long.

Since equation (1) includes but two variables, the independent variable, intensity, and the dependent variable, exposure time, it follows that if one were to know beforehand the intensity of the radiation with which a roentgenogram is to be exposed one might easily calculate algebraicly the proper exposure time which would produce a roentgenogram of maximum diagnostic quality. Until recently satisfactory instruments with which the intensity of roentgen rays might be measured directly have not been available and it has been necessary to resort to indirect methods for determining roentgenographic exposure factors.

The method most commonly in use today determines exposure technique from the thickness of the anatomical structure under examination. This method is based upon the principle that the intensity of the radiation falling upon a roentgenographic film is dependent in part upon the thickness of the tissue penetrated by the roentgen rays. Intensity, however, is also governed by the absorption characteristics of the tissues, characteristics that are not necessarily reflected in measurements of tissue thickness. Indeed, it is rather un-

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closely linear, it is evident that in a roentgenogram composed of a complexity of densities, the relationship between average density and the average exposure received by the film is given by the equation,

$$\bar{D} = \sigma(\bar{G}t - \epsilon) \tag{d}$$

where $\bar{D}$ is the average density of the roentgenogram, and $\bar{G}$ is the average intensity of the radiation falling on the film.

We have seen that the average density at which optimum roentgenographic quality occurs is 0.9. When this value is substituted for D in equation (d) and terms are rearranged,

$$\bar{G}t\left(\frac{\sigma}{0.9+\epsilon\sigma}\right) = 1 \tag{e}$$

It is clear from its derivation that equation (e) specifies the conditions for correct roentgenographic exposure.

Since the value of

$$\left(\frac{\sigma}{0.9+\epsilon\sigma}\right)$$

is a function of the sensitivity of the film, it may be conveniently called the film speed factor and represented by the symbol, s_e. Equation (e) then becomes

$$t = \frac{1}{s_e \bar{G}} \tag{f}$$

The roentgenographic exposure meters,[5,6] developed in this laboratory, have been designed to measure directly the average effective intensity of the radiation with which a film is to be exposed; i.e., meter deflections, M, are proportional to values of G. Thus,

$$M = SG \tag{g}$$

where S is a constant whose value is dependent on the sensitivity of the exposure meter. When G is eliminated from equations (f) and (g),

$$t = \frac{S}{s_e M} \tag{h}$$

Correct exposure time, therefore, may be calculated directly from exposure meter readings when the sensitivity of the instrument and the speed factor of the film to be exposed are known.

If the exposure meter includes a sensitivity control whose dial is calibrated in terms of film speed factor, so that

$$S = cs_e \tag{i}$$

where c is a proportionality constant, equation (h) becomes,

$$t = \frac{c}{M} \tag{j}$$

when the dial of the sensitivity control is adjusted to the position corresponding to the speed factor of the film to be exposed. Equation (j) indicates that a given deflection of the exposure meter always specifies the same exposure time regardless of the type of film being used. Therefore, the scale of the instrument may be calibrated directly in units of exposure time (see Fig. 7) and mathematical computations for the determination of t thereby become unnecessary.

From the foregoing it is evident that roentgenographic exposure meters place the determination of roentgenographic exposure technique on a direct, quantitative basis, free from the discrepancies of the tissue-thickness method of exposure calculation

usual to find two chests of equal thickness with identical absorption characteristics. Accordingly the tissue-thickness method of exposure calculation cannot be expected to yield consistently uniform results. Even with the refinements proposed by Weyl and Warren[11] where the factor of body build is taken into consideration, the method is not entirely satisfactory since its inherent objections are still present. In spite of this, however, the method has found almost universal usage principally because none better has been available.

The inadequacy of the tissue-thickness method to provide adequate control of exposure is well shown in the following analysis of 100 chest roentgenograms picked at random from our files and exposed according to the method between the dates of March 1, 1942 and April 1, 1942. These films were subjected to densitometric examination and the minimum and maximum significant densities (hilar regions and peripheral lung fields respectively) of each roentgenogram measured. From these data, the average densities* of the films were determined and the results examined statistically. The standard deviation in average density of the films was calculated from the equation,

$$\text{S.D.} = \pm\sqrt{\frac{\Sigma(\bar{x}-x)^2}{n-1}} \qquad (2)$$

where $\bar{x}$ is the mean average density of all of the films, x is the average density of a single film, and n is the number of films examined, and was found to be ± 0.20 of a mean average density of 0.86; that is, the variation in the average density of chest films exposed according to the tissue-thickness method of exposure calculation, in our hands at least, is considerably greater than that desired (i.e. considerably greater than ± 0.1 of 0.9).

* The average of the minimum and maximum densities of a roentgenogram does not necessarily represent the roentgenogram's true average density. In most cases, however, it does represent a close approximation. The measurement of true average density is a long and tedious operation and is hardly warranted in a study of this kind.

This variation cannot be ascribed entirely to errors in exposure calculation. Some variation must be attributed to differences in the manner in which the films were processed, to differences in the operating characteristics of the roentgen machine and to differences in the sensitivities of the roentgenographic material. In order to estimate the variation contributed by these factors, 20 chest roentgenograms exposed with identical technical factors were made on a particular individual. These films were developed under routine darkroon conditions, one each day during the ensuing twenty days, examined densitometrically, and the results studied statistically. The standard deviation in the average density of these roentgenograms was ± 0.12 of a mean average density of 0.92. Most of this variation probably may be ascribed to the process of developing.

If it be assumed that the variation in average density caused by factors other than errors in exposure calculation is the same in the 100 films as that in these 20 films (it is a reasonable assumption since identical roentgenographic and darkroom apparatus were used in the two cases), it is possible to calculate the standard deviation in the average density of the 100 films contributed by the tissue-thickness method of exposure calculation alone by means of the equation,

$$x = \pm\sqrt{z^2 - y^2} \qquad (3)$$

where x is the standard deviation due to a single factor, y is the standard deviation due to the remaining factors, and z is the standard deviation due to all factors collectively. When values of 0.20 and 0.12 are substituted for z and y respectively in equation (3), the value of x is ± 0.16. Such a variation clearly indicates that the tissue-thickness method of exposure calculation does not provide adequate control of roentgenographic exposure.

Since indirect methods of exposure calculation are unsatisfactory, it is evident that the solution of the problem of exposure control lies in the development of roentgen-

ray intensitometers with which the intensity of the radiation to be received by roentgenographic films may be measured directly. Several such devices[2,3,8,9,10] have been described during the past decade but most have been rather ineffective due to their critical operating characteristics.

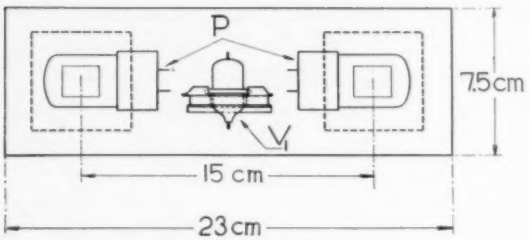

Fig. 5. Layout of radiation detector: P, type 929 phototubes; V_1, type 954 amplifier tube. Dimensions of light-proof case in which these components are mounted are as indicated. The positions of the fluorescent screens overlying the phototubes are shown in dotted outline.

Also it has been recently shown[6] that satisfactory operation of a roentgen-ray intensitometer can only be expected when the response of the instrument throughout the roentgen-ray spectrum is identical to those of films exposed either with or without intensifying screens. As far as can be determined, no attempt was made to fulfill this criterion in these early instruments.

Recent advances in the design of photoelectric equipment have made it possible to overcome most of the difficulties encountered in the development of early roentgen-ray intensitometers and it may be confidently stated that reliable instruments are now entirely practical. Since the main function of these devices pertains to the determination of roentgenographic exposure technique, they have been called roentgenographic exposure meters.

During the past two years, two types of roentgenographic exposure meters have been developed in this laboratory. One [5,6] is similar in basic design to the photographic exposure meters with which everyone is familiar and includes as essential components a radiation detector comprising a small fluorescent screen, a phototube and a vacuum tube amplifier, and a second unit including a microammeter and a power supply. When roentgen rays impinge on the radiation detector, the screen fluoresces

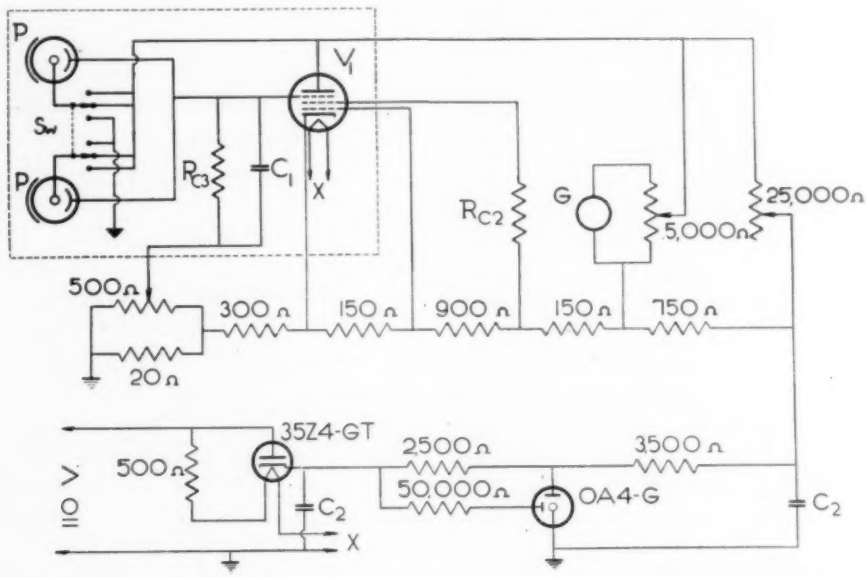

Fig. 6. Circuit diagram of exposure meter suitable for use in roentgenography of the chest: P, type 929 phototubes; Sw, double pole, three position switch; V_1, type 954 amplifier tube; C_1, 500 micromicrofarad condenser; C_2, 16 microfarad condensers; R_{C2}, 1,500 ohm resistor; R_{C3}, 2×10^9 ohm resistor; G, 0–50 microammeter.

and in response to this radiation the phototube conducts a small electric current, the magnitude of which is proportional to the effective intensity of the roentgen radiation. This current is amplified and then recorded by the microammeter. Thus, meter deflections are proportional to the intensity of the roentgen rays.

A diagram of a typical radiation detector suitable for use in chest roentgenography is shown in Figure 5; the device includes the two phototubes, *P*, each scanning separate lung fields, and the amplifier tube, V_1. The phototubes are separated a distance of approximately 15 cm. and in front of each is a Patterson type "B" fluoroscopic screen (shown in dotted outline), 2 inches square. In order that the response of the exposure meter may be independent of roentgen-ray quality, aluminum filters, 0.5 mm. in thickness, overlie the screens. The detector unit is mounted directly behind the cassette changer of the roentgen machine in such a position that radiation from the fields shown in dotted outline in Figure 1 is projected on the fluorescent fields. These fields seem sufficiently large to be representative of the diagnostic areas of most chests.

A circuit diagram of the exposure meter is shown in Figure 6. It is similar to circuits previously published with the exception that the three-way switch, *Sw*, is included. This device permits the operator to measure the intensity of the radiation from both fields simultaneously or from each field separately. With the latter technique correctly exposed roentgenograms of either lung field may be obtained in patients with unilateral disease. The condenser, C_1, provides a ballistic-like action to the microammeter so that roentgenometric measurements may be taken with extremely short exposure times. The 5,000 ohm potentiometer in the amplifier plate circuit serves as a film speed control: the 500 ohm potentiometer in the control grid circuit provides zero adjustment of the microammeter.

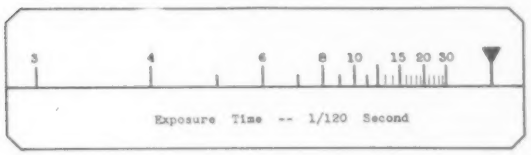

Fig. 7. Microammeter scale used in exposure meter designed for roentgenography of the chest. Such a scale permits the operator to determine roentgenographic technique without consulting charts or mathematical formulae.

The scale of the microammeter is calibrated directly in terms of exposure time (see Figure 7) rather than in arbitrary units of intensity so that the operator may determine roentgenographic exposure technique directly from exposure meter readings; mathematical computations and consultations of graphs and charts are therefore unnecessary.

To use the exposure meter, the patient to be examined is placed before the cassette changer and the roentgen machine adjusted to suitable kilovoltage and milliamperage settings. The film speed control is then rotated to the proper speed factor of the film to be exposed, the zero adjustment control turned to the position in which the microammeter needle rests at the reference line (see Fig. 7) at the right of the scale, and the switch, *Sw*, thrown to its intermediate setting. With the chest in full inspiration a test exposure of 6/120 second is made and the deflection of the microammeter needle observed. This deflection indicates the exposure time which will insure correct exposure of a film when exposed with a roentgen beam identical to that with which the roentgenometric reading is taken. If it is desired to measure each lung field separately, the switch *Sw* is thrown to its right and left positions in turn and test exposures of 12/120 second made. Again correct exposure times will be indicated by the deflections of the microammeter needle. The test exposure time employed in the latter technique is twice the former because only one phototube is operating under this condition. When the roentgenometric observations have been

completed films are placed in the cassette changer and the roentgenographic exposures made after the timing mechanism of the roentgen machine has been suitably adjusted. In order that it may not be necessary to disturb the patient when placing films in the cassette changer it has been

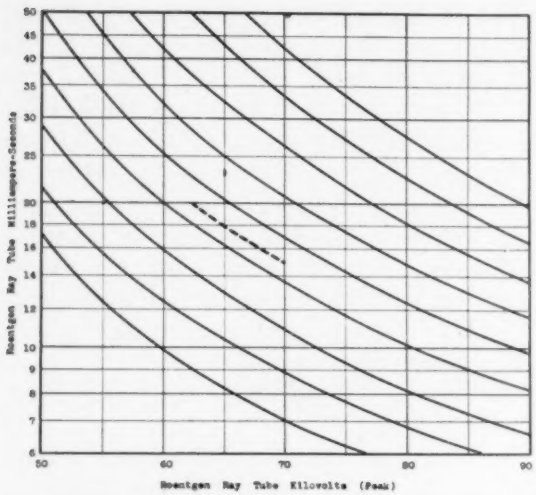

Fig. 8. Exposure meter readings specify roentgenographic technique in terms of exposure time. Some roentgenologists, however, prefer to control exposure through changes in kilovoltage. This chart permits conversion from one system to the other (see text for method of use).

found desirable to modify the cassette carriers so that side loading of films is possible.

It will be observed that the control of exposure in the roentgenometric method is obtained through changes in exposure time. Many roentgenologists, however, prefer to effect this control by changing kilovoltage. The chart shown in Figure 8 permits one to determine roentgenometric technique in terms of kilovoltage from roentgenometric readings. The following example will serve as an illustration of its use: Let us suppose that an exposure meter reading taken at 70 kv. (peak) indicates a technique of 15 milliampere-seconds and it is desired to find the kilovoltage which will provide an equivalent exposure at 20 ma-sec. A point corresponding to 15 ma-sec. and 70 kv. (peak) is chosen on the chart and an imaginary line drawn through it parallel to the curve immediately above (see dotted line). The desired kilovoltage is indicated by the intercept of this imaginary line with the 20 ma-sec. ordinant; that is, 62.5 kv. (peak). This chart may be used with any four-valve roentgen machine in which the target-film distance is 6 feet. It is of particular value when an impulse timer is not available. If such a system is at hand, however, it is simpler to control roentgenographic exposure entirely through changes in exposure time.

Figure 8 was prepared from data obtained by taking exposure meter readings through 2.0 mm. of aluminum and various thicknesses of Masonite pressdwood, with kilovoltages ranging from 50 to 90 kv. (peak). The thickness of aluminum employed has approximately the same absorption as an average thoracic cage and the pressdwood approximately the same absorption as lung, muscle, and other fibrillar tissue. The pressdwood was arranged directly above the exposure meter so that scattered as well as direct radiation was received by the instrument. Thus conditions essentially similar to those encountered in roentgenography of the chest were obtained.

The technical factors employed in the exposures of the roentgenograms reproduced in Figure 9 were obtained from data provided by the chart. Kilovoltages ranged from 50 kv. (peak) in *A* to 80 kv. (peak) in *D*. The similarity in appearance of the several films is apparent.

Although the performance of the exposure meter just described has proved eminently satisfactory it has the disadvantage that two exposures, one for making the roentgenometric reading and one for exposing the film, are necessary for every roentgenogram made.

This objection is effectively overcome by the second type of exposure meter,[7] a photoelectric timing mechanism, with which roentgenographic exposure is controlled automatically. The instrument includes a radiation detector employing a multiplier-type phototube and a thyratron-

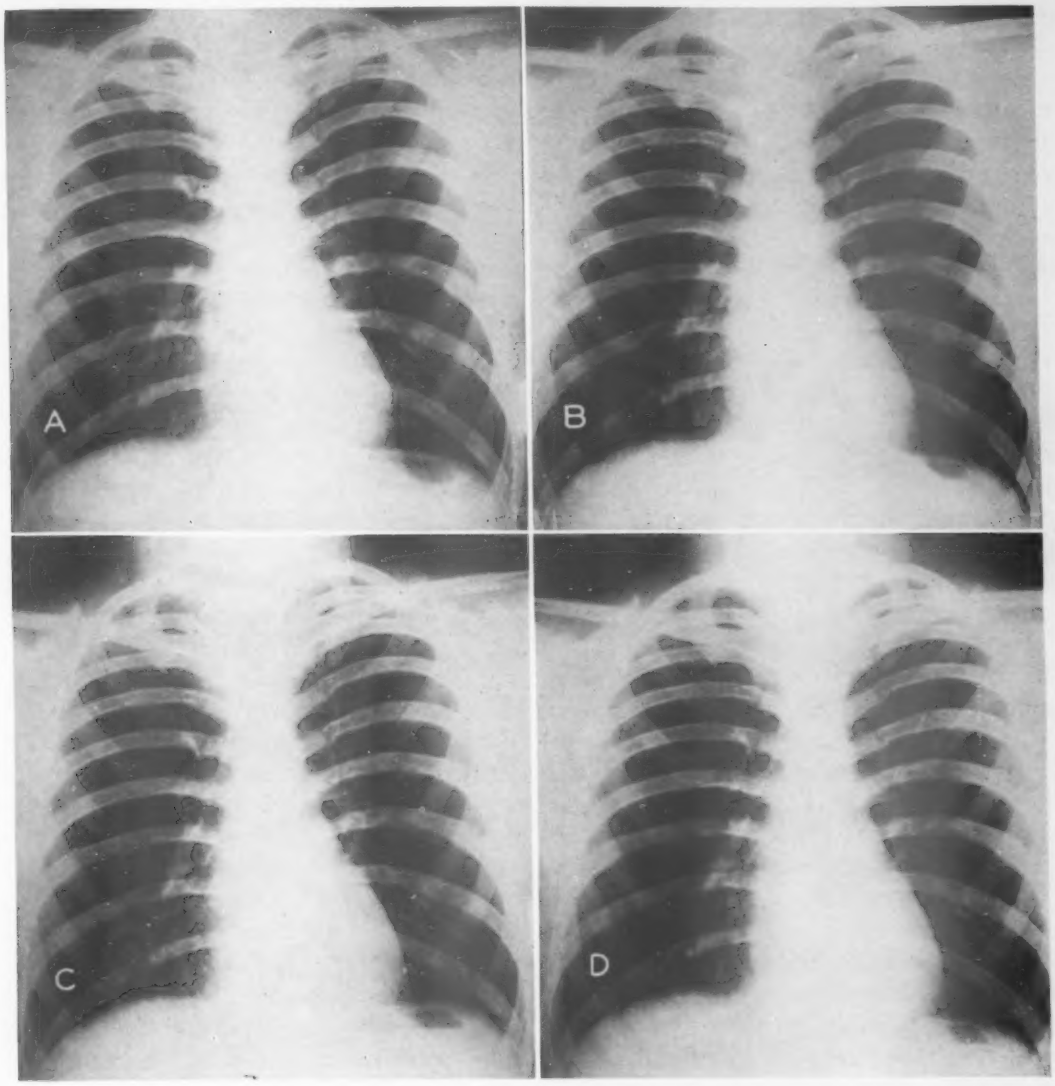

Fig. 9. Series of roentgenograms of the chest in which exposure factors were determined from data provided by Figure 6: *A*, 50 kv. (peak), 48 ma-sec.; *B*, 60 kv. (peak), 24 ma-sec.; *C*, 70 kv. (peak), 16.7 ma-sec.; *D*, 80 kv. (peak), 12 ma-sec. The similarity of the average densities of the various roentgenograms illustrates the validity of Figure 8.

activated relay system. To operate a roentgen machine equipped with this device, films are placed in the cassette changer, suitable kilovoltage and milliamperage settings chosen, and the exposure switch of the roentgen machine closed. When the proper quantity of radiation has been delivered to the film the photoelectric timing mechanism breaks the roentgen-ray circuit and the exposure is terminated automatically. All calculations of exposure technique and critical adjustment of roentgenographic equipment are unnecessary. It appears that the phototimer is the ultimate in exposure control devices. However, multiplier phototubes necessary for its operation will not be generally available until after the war is over.

In routine roentgenographic practice exposure meters in this laboratory have

provided excellent control of roentgenographic exposure. In 100 films of the chest exposed according to roentgenometric measurements and picked at random from our files, the standard deviation in the average density of the films was found to be only ±0.06 of a mean average density of 0.89. In this series of films an aluminum ladder was roentgenographed in the corner of each film; this permitted a direct calculation of the standard deviation contributed by the roentgenometric method. It is evident from these results that the roentgenometric method of exposure calculation provides almost a three-fold decrease in the variation of the average density of chest roentgenograms over that obtained with the tissue-thickness method.

III. CONTROL OF THE PROCESS OF DEVELOPMENT

It must not be assumed that roentgenographic exposure meters provide the entire answer to the several problems relating to the control of roentgenographic quality. We have seen that the variation in the average density of chest roentgenograms contributed by the roentgenometric method is ±0.06, but it has also been pointed out that variations due to factors other than exposure calculation and principally connected with the process of development amount to ±0.12. When these two figures are added statistically by means of equation (3) it is found that the standard deviation in the average density of chest roentgenograms made with exposure meter control and developed under routine darkroom conditions is ±0.14. This represents only a moderate improvement over the variation of ±0.20 in roentgenograms made according to the tissue-thickness method of exposure calculation. It is obvious then that if the potentialities of exposure meters in the control of roentgenographic quality are to be fully utilized the methods of processing films must be substantially improved.

In most roentgen-ray laboratories roentgenograms are developed by the method of visual inspection whereby the films are examined periodically before the darkroom red-light during development. As long as exposures are calculated from measurements of tissue thickness, it is almost imperative that this method be employed if overexposed films are to be prevented from becoming excessively dark. On the other hand, darkroom personnel are poor judges of roentgenographic quality due, among other things, to the lighting conditions under which they work; accordingly the method is likely to cause more variation in roentgenographic quality than is desirable.

We have observed a considerable reduction in the variation in average density of chest roentgenograms when development is conducted on a strict time-temperature schedule. In an experimental test in which 20 roentgenograms of the chest were made on a particular individual, exposed with constant exposure and processed one each day over a period of twenty days under time-temperature control, the standard deviation in the average density of the films was ±0.07, or much less than the standard deviation of ±0.12 observed previously.

In the past, strict adherence to a time-temperature method of development has been rather impractical due to the large variation in the exposures received by films exposed according to the tissue-thickness method of exposure calculation. With roentgenometric control of exposure, however, this situation no longer exists. Chest roentgenograms exposed under roentgenometric control, where the resulting deviation is ±0.06, and processed by a time-temperature method, where the resulting deviation is ±0.07, demonstrate an overall deviation of ±0.09. Such a variation is well within the limits which may be tolerated (i.e., less than ±0.10); indeed, roentgenograms showing as little variation as this are remarkably uniform by present-day standards.

SUMMARY

The control of roentgenographic quality in roentgenograms of the chest involves

two principal problems: (*a*) the regulation of exposure, and (*b*) the control of the process of developing. Adequate regulation of exposure may be obtained through the use of recently developed roentgenographic exposure meters. Adequate control of the process of developing can only be expected when the time-temperature method is employed. When roentgenographic quality is controlled by these means chest roentgenograms of excellent uniformity and quality may be obtained routinely.

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DISCUSSION

Dr. George C. Henny, Philadelphia. I would like to open this discussion very briefly by saying that the excellence of the piece of work accomplished by Dr. Morgan is indeed very evident to one who has been seriously interested in building an exposure meter. Other people have tried to devise these exposure meters, particularly because many technicians have been clamoring for them, but there have been various difficult problems that had to be solved before they were satisfactory. One of the main problems was to obtain a response of the exposure meter that was parallel to the response of the roentgen film or the film and screen combination. This has been beautifully done in Dr. Morgan's meter, as you can well see by the roentgenograms shown in his exhibit for different kilovoltages using the same part.

Most technicians regulate their technique by varying kilovoltage according to the thickness of the patient. In most of Dr. Morgan's work, however, the kilovoltage is left constant and the time is varied according to the thickness of the patient. One would think that the contrast resulting in the finished roentgenograms might suffer by this technique, and yet it is interesting to note on Dr. Morgan's roentgenograms in his exhibit how little the contrast has suffered when the kilovoltage is raised. The exposure meter kept the average density of the films remarkably constant.

SEMINOMA OF THE TESTIS FROM THE STANDPOINT OF ROENTGEN TREATMENT*

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INTRODUCTION

TUMORS of the testis are important lesions. This fact is attested to by the circumstance that 215 references to this condition appeared in the "Quarterly Cumulative Index Medicus" from 1934 to 1938, inclusive. A most casual and superficial review of the literature on tumors of the testis will indicate how confused and how contradictory this subject is.

Since the treatment of most testicular tumors, particularly the treatment of seminoma of the testis, usually falls to the therapeutic radiologist, this study was undertaken to review critically and to summarize present knowledge of these tumors in order to aid the radiologist in the care of patients who have seminomas of the testis.

We have chosen to study seminoma of the testis in all of its clinical aspects for it is the most common testicular neoplasm and it has a number of features in common with testicular tumors of other types. It is said, nevertheless, to have certain characteristics which distinguish it from other testicular tumors and from other malignant neoplasms arising elsewhere in the body. We shall attempt to determine these characteristics.

There are two principal controversial views about the pathogenesis of seminomas of the testis. For example, Langhans, Wilms, Ewing,[38] and Oberndorfer expressed the opinion that all malignant tumors of the germinal epithelium of the testis are related but produce varying pathologic manifestations and thus, in turn, different histopathologic appearances. The second view, held by Birch-Hirschfeld, Chevassu,[20] Frank, Sakaguchi, Bell, Geist and Thalhimer, Schultz and Eisendrath, Innes, Harvey and Dawson, McDonald and associates,[73] and Broders[17] is that seminoma of the testis is a separate entity. Largely as a result of this difference of thought, the literature of the subject is confusing and therefore it is becoming increasingly difficult to evaluate certain aspects of seminomas of the testis, particularly with reference to treatment.

It is not our purpose to take sides in the controversy about the pathogenesis of testicular tumors, but we do wish to determine from other points of view what characteristics, if any, distinguish seminomas of the testis from other testicular neoplasms. These points have been gathered from a review of the records, physical findings, clinical behavior and response to roentgen therapy in 103 proved cases of seminoma of the testis encountered at the Mayo Clinic. We intend, also, to review the histopathologic appearance in these cases of seminoma of the testis, to present several of the major classifications of testiculor tumors, to discuss the literature of the biologic (hormonal) characteristics of seminoma of the testis and to review the pertinent literature on the radiotherapy of this testicular tumor. From this material we hope to be able to correlate some of the divergent conceptions of the subject.

Testicular tumors were mentioned in medical literature as early as 1696 by St. Donat, but significant attempts to classify these tumors were not made until the be-

* Thesis submitted by Dr. Nash to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Radiology.

ginning of the present century. Chevassu,[20] in his classic monograph published in 1906, coined the term "séminome," now anglicized to "seminoma," to signify a tumor of the seminal or germinal epithelium of the testis. The increase in the literature of tumors of the testis has paralleled the development of roentgen therapy, and recent advances in endocrinology have also contributed immensely to the literature on the subject.

INCIDENCE OF SEMINOMAS OF THE TESTIS

The incidence of seminomas of the testis can be determined from their relative occurrence among testicular tumors of all kinds. In Göttingen, Blümel found 22 patients who had testicular tumors out of 40,000 general hospital registrations. In Stockholm, Grevillius recently collected 36 cases of testicular tumors from 2,752 cases of tumor occurring among males and in another group from Upsala, 8 in a series of 890 cases of tumor among males. In America, Tanner stated in 1922 that testicular tumors occurred once in every 2,000 male admissions to American hospitals. Dean,[26] in 1935, stated that testicular tumors represented 1.008 per cent of all tumors of both sexes from the ages of one to seventy years, and that 2.09 per cent of all malignant tumors of males were primary in the testis.

In regard to the relative incidence of seminomas of the testis, Cabot and Berkson found that seminoma occurred in 59.2 per cent of proved cases of testicular tumors. Grevillius, in his study of 189 malignant testicular tumors, reported that seminomas accounted for 112, which incidentally is the identical percentage of 59.2 of Cabot and Berkson. Geist and Thalhimer found the incidence of seminomas to be 61.5 per cent, Herman placed the figure at 65 per cent, Sakaguchi at 65.6 per cent and Blefari-Melazzi at 70 per cent. We found that seminoma of the testis occurred once in every 8,957 registrations at the Mayo Clinic.

CLASSIFICATION OF TESTICULAR TUMORS

Since this presentation will consider in some detail the roentgen therapy of seminomas, some of their pathologic aspects will be presented in detail so that various terms used with reference to testicular tumors may become more familiar to the reader. As stated previously, there are essentially two schools of thought in regard to the classification of testicular tumors. Ewing's[38] theory that all common testicular tumors arising from the germinal epithelium of the testis merely represent different degrees of development of the constituents of a teratoma has been accepted widely. Opposed to Ewing are those who are of the opinion that any of the constituents of the testis may undergo malignant change and so may produce tumors which represent the parent tissue, either in a relatively pure form or in production of a heterologous neoplasm. Ewing[38] stated:

> In the testis, more notably than in any other organ, it is possible to maintain a single embryonic origin of the great majority of tumors. It appears that all the common and nearly all the rarer tumors of this organ arise from totipotent sex-cells, and that the monodermal forms of these growths represent one-sided developments of tridermal teratomas.

Obviously, it is beyond the scope of this study to try to settle the controversy over classification of testicular tumors, and certainly we are not in a position to refute or affirm the views of Ewing. For the purpose of this presentation, however, we do not think it out of order to call attention to a familiar criticism of his classification. Most physicians have been taught to regard the word "teratoma" as a general term specifically applicable to a monster growth and more loosely to a tumor which exhibits more than one of the primitive embryonic germ layers. As used by Ewing,[38] it is a term applied to most testicular tumors. By the nature of the function of the germinal epithelium of the testis, it is difficult to refute the statement of Ewing that all testicular tumors represent a one-sided development of totipotent sex cells.

Ewing[38] designated all the common tumors of the testis under the heading of "teratoma" and classified them as follows:

I. Adult embryomas or teratomas. The majority of these are benign.
II. Teratoid, embryoid, or mixed tumors. These tumors are malignant.
III. Embryonal tumors of the testis, including sarcoma of the testis, seminoma (Chevassu), and embryonal carcinoma with lymphoid stroma.
IV. Miscellaneous tumors of the testis and associated structures; these tumors are rare.

The influence of Ewing's[38] classification is apparent if the literature on tumors of the testis is consulted, particularly that of American writers who generally have accepted it.

Various authors[8, 11, 17, 20, 47, 63, 73, 96, 98] were not in accord with this method of classification. Some have subscribed to what seems a less dogmatic stand. Oberndorfer, whose theory of the origin of testicular tumors is not unlike Ewing's[38] in some respects, calls seminoma of the testis the "specific malignant testicular tumor" because of certain characteristics which we shall discuss later. Hamburger, Bang and Nielsen pointed out their belief that the majority of testicular tumors are neither seminomas nor a tumor of another type, which they chose to call "mixed epithelioma of the testis." These mixed epitheliomas, they stated, are second only to seminoma in frequency of occurrence, and contain tissue other than epithelium but with a predominance of that tissue. There are islands of other cells in these mixed epitheliomas, notably cartilage, and for reasons given in their published works, they stated that the nonepithelial tissues represented development of totipotent sex cells, which took place before the cancerous epithelial changes in the seminiferous tubules. These authors thus accept the teratomatous origin of mixed epithelial tumors; however, they are of the opinion that seminoma of the testis is a definite nosologic entity. This opinion, stated in other ways, seems to be accepted by that group which opposes the general contention of Ewing.[38]

Hamburger, Bang and Nielsen's classification is as follows:

I. Tumors of ordinary fibrous tissue (fibromas, sarcomas, and so forth).
II. Tumors of interstitial cells (hyperplasia and epitheliomas).
III. Tumors of the excretory ducts.
  A. From rete testis: adenomas, malignant adenomas.
  B. From embryonal inclusions of the wolffian system: wolffian epitheliomas.
IV. Tumors from heterotopic inclusions. (Inclusions of suprarenal glands.)
V. Tumors of the sex cells ("germinal line").
  A. From the gonocytes, embryonal cords and embryonal inclusions of these:
    1. Teratoid ("dermoid") cyst.
    2. Teratoid mixed polycystic tumor.
      a. Histologically benign.
      b. Histologically malignant.
        (Undergroups: chondroma, osteoma, chondrosarcoma).
    3. Adenoma of the testis, embryonal seminoma, embryonal mixed epithelioma, etc. (Most frequently in the undescended testis.)
  B. From the cells in the testicular tubules:
    1. Seminoma of the testis.
    2. Mixed epithelioma of the testis.
    3. (Mixed polycystic tumors?)
VI. Other tumors. (For example, the bilateral lymphosarcoma of children.)

According to these authors mixed epitheliomas often are designated by others as "embryonic epithelioma" or similar terms. The epithelial cells appear to have a particular capacity for syncytial differentiation and hence regions of the tumor resemble chorio-epithelioma, although they do not correspond throughout to the female type of chorio-epithelioma. We shall not discuss the detailed theoretical considerations in regard to the sites of origin of the various tumors, but will state that these authors diagnose as seminoma those tumors which histologically appear typical, and that the mixed epitheliomas present a number of histologic variations. We have presented this classification mainly in order

to elucidate the discussion of the production of hormone in the urine of patients who have testicular tumors, particularly seminomas of the testis.

It seems to us that the classification of testicular tumors into homologous and heterologous types originated with a publication by Schultz and Eisendrath in 1921. We shall not review their work here except to state that these authors introduced the term "spermatocytoma," which is the tumor we speak of as seminoma of the testis. Hinman's[58] method of placing testicular tumors into two large groups, homologous and heterologous, seems to represent the subject in a somewhat different, although satisfactory, manner. His classification is as follows:

I. Homologous
  A. Benign
    1. Epithelial
      a. Adenoma of the seminal tubules
      b. Misplaced ectoderm
    2. Mesoblastic
      a. Interstitial cell tumors (probably not true tumors but merely hyperplasia [Ewing])
      b. Tumors of connective tissue
      c. Misplaced mesonephric tissue
  B. Malignant
    1. Epithelial
      a. Seminoma (unicellular)
    2. Mesoblastic
      a. Sarcoma (lymphosarcoma, myosarcoma)
    3. Tumors of adrenal rests (small cell adenocarcinoma derived from adrenal tubules, occurring in men of middle age and running a slow course [Ewing, Bell, Stevens])

II. Heterologous
  A. Benign
    1. Dermoid cysts (simple and complex)
    2. Organized embryomata
  B. Malignant (mixed cell tumor)
    1. Adult teratoma (with few or early malignant changes)
    2. Malignant teratoma (embryonal carcinoma) occurs as complex varieties of fairly uniform to very mixed tumors.
      Uniformity
      a. Hypoblastic (embryonal adenocarcinoma)
      b. Mesoblastic (embryonal carcinoma with lymphoid stroma)
      c. Epiblastic (basal cell epithelioma, etc.)
      d. Trophoblastic (chorionepithelioma)

III. Tumors which cannot be classified.

This classification is useful because Hinman and his co-workers[58–62] have contributed much to the literature on testicular tumors and have had some influence on the opinions of others.

Herman has a similar classification in his recent textbook. Included among malignant homologous testicular tumors are the seminoma of Chevassu,[20] the embryonal carcinoma of Ewing[38] and the spermatocytoma of Schultz and Eisendrath.

Ferguson,[43] who has contributed much to the literature on testicular tumors, recently proposed a simple classification of these neoplasms. He divided testicular tumors into two groups, the first is "teratoma testis simplex," and includes the seminoma of the testis and the embryonal carcinoma; the second group is "teratoma testis complex" and includes the heterologous growths.

Grevillius' classification of testicular tumors, made after an extensive study of malignant testicular tumors, is as follows:

I. Pure tumors of connective tissue. (Sarcoma, fibroma and so forth.)
II. Tumors of interstitial cells
III. Tumors of the excretory ducts. (Adenoma, adenocarcinoma.)
IV. Tumors of the seminal epithelium. (*Geschlechtszellen.*)
  A. Seminoma.
  B. Mixed tumors.
    a. Mature or adult type.
    b. Immature or embryonic tumors in which eventually a certain histologically benign or malignant tissue predominates.
  C. Carcinoma of the testis.
    a. Undifferentiated.
    b. Adenocarcinoma.

D. So-called chorio-epithelioma of the testis.
E. Adenoma of the tubules. Hypothetic site of origin in the seminiferous tubules.

V. Tumors of heterologous inclusions.
VI. Other tumors.

Broders[17] classified the tumors arising from seminal epithelium by his well known method of grading of the malignancy index. Since the classification refers only to tumors of the germinal epithelium, it seems to us ideal, for it is inclusive, simple and useful. It is as follows:

I. Teratoma.
A. Benign. Adult type.
B. Malignant.
II. Adenocarcinoma of the testicle. This is not a seminoma and there is no heterologous tissue present to suggest an origin from a teratoma.
III. Adenocarcinoma of the seminoma type. These all are Grade 4 malignancies.

Adenocarcinomas of the testis, listed in Group II of Broders' classification, display definite acini and vary in degree of differentiation from Grades 1 to 4. Adenocarcinoma of the seminoma type is the tumor meant when we use the term "seminoma of the testis." Seminomas of the testis are adenocarcinomas because of their origin from glandular tissue. By the fundamental principles of Broders'[16] original plan of grading tumors, seminomas of the testis, because of their microscopic characteristics, necessarily fall into the Grade 4 group of malignancies. There is a degree of similarity almost approaching identity between the classifications of tumors arising from the seminal or germinal epithelium of the testis proposed by Grevillius and by Broders.[17] These classifications were drawn up independently, however.

Pruszczyński, in 1933, subdivided seminomas into four types. The first of these is the mesoblastic type, which occurs in ectopic testes or in pseudohermaphrodism. The tumor displays round cells with dark protoplasm; these cells arise in small spermatoblasts which are the predecessors of spermatogonia. The second is the spermatogonic type and arises from these structures. Pruszczyński referred to Peyron's discovery of crystalloids in certain spermatogonia and identified these crystalloids in some seminoma cells. The third type is derived from the Sertoli cells, and he was of the opinion that seminomas may arise from these cells. Finally the fourth, or mixed, type of seminoma was added. This division is somewhat academic and any further consideration of the third type particularly by us would involve controversial subjects. McDonald[73] discussed the subdivision of seminomas and expressed the opinion, as did Chevassu,[20] that the seminal or spermatogonic type is the tumor spoken of as seminoma.

Most authors classify as seminomas of the testis both the homologous, malignant, monocellular, epithelial testicular tumor and the tumor which in some classifications is described as a heterologous, malignant teratoma of mesoblastic origin or an embryonic carcinoma with lymphoid stroma. The significance of lymphoid stroma will be discussed in another portion of this paper. It should be remembered that occasionally a pathologic diagnosis of sarcoma of the testis is made, but in the majority of cases the lesion is in reality a seminoma. The difficulties of differentiating a sarcoma from an undifferentiated epithelial tumor is too well known to be more than mentioned.

McDonald[73] pointed out why Broders' classification of testicular tumors is logical and fitting. Since seminomas have their origin in the seminiferous tubules of the testis they actually are adenocarcinomas. All seminomas in our series of 103 consecutive proved cases were graded 4 according to Broders'[16] method of classification. By definition and by the description of Chevassu,[20] Bell and Grevillius, the tumor is highly undifferentiated and thus is graded 4.

Whatever variations there may be, the question finally resolves itself into the tenet that Broders'[17] classification of tumors of the testicular germinal epithelium is

sufficiently inclusive to embrace all types of tumors of that tissue, and is subdivided to the extent that the differences in microscopic appearance and in clinical behavior of these tumors, together with their treatment, are specifically indicated. Further subdivision is superfluous and, in most cases, impossible microscopically. A general tendency toward simpler classification has been noted in our study of the literature of testicular tumors. This tendency, when it becomes more universal, will aid in correcting the confusing and contradictory views now existing. For these reasons, we are of the opinion that Broders'[17] classification is most suitable and we have adopted it in our study.

In order to summarize and clarify terminology, it should be remembered that the seminoma of Chevassu or adenocarcinoma, Grade 4 (Broders'[17] classification), of the seminoma type, is identical with the embryonal carcinoma of the testis (Ewing[38]), the pure monocellular seminoma (Hinman[58]), the embryonal carcinoma with lymphoid stroma (Ewing[38]) and the spermatocytoma of the testis (Schultz and Eisendrath). Bell has accepted the term "seminoma" as most suitable for this tumor, since it is inclusive of the variations which can occur.

Every classification of testicular tumors that has been published cannot be discussed, but we feel that the foregoing should correlate the terminology applied to seminomas of the testis.

PATHOLOGIC FEATURES OF SEMINOMAS OF THE TESTIS

Gross Appearance. The size of seminomas varies to a certain extent with the duration of the disease. This statement does not hold absolutely true, for often the metastatic manifestations of seminomas of the testis are present before the primary tumor is readily detectable on clinical examination. Characteristically, the tumor varies in size from that of a hen's egg to the size of a child's head. Usually it is stated to be twice the size of a normal testis. To illustrate the variation, one may find some tumors in our series of cases were spherical masses which measured 1.0 cm. in diameter and others approached an ovoid shape which measured 10.0 by 13.0 by 19.0 cm. Typically, the shape of the normal testis is preserved until late. A certain number of these tumors are associated with hydrocele, but often the serosal surfaces are adherent. The surface of a seminoma generally is smooth, but often it is lobulated with a coarsely pitted surface. The tunica albuginea is intact in the majority of cases and displays a network of dilated veins. Generally, the tumors are stated to be of an elastic, uniform consistence; occasionally they are fluctuant and only rarely are they said to be firm or hard on gross examination. Until the tumor is large enough to interfere mechanically with the epididymis, that structure usually is intact. The cut surface of the fresh specimen is homogeneous and yellowish or yellow white; at times it is grayish. Occasionally it is lobulated. Regions of necrosis and hemorrhage frequently are seen on the cut surface

In a typical seminoma of the testis a trabeculated appearance is apparent (Fig. 1*a*). In a teratoma of the testis the predominating histopathologic appearance is that of an adenocarcinoma (Fig. 1*b*). Figure 1*c* illustrates an adenocarcinoma, Grade 4, which is not a seminoma and apparently not a teratoma.

Microscopic Appearance. According to the description by Chevassu,[20] and the classification of this tumor by Broders,[17] seminoma of the testis is characteristically highly cellular and undifferentiated. In fixed sections, the cells are round or polyhedral, with large, deep-staining nuclei and are scant in cytoplasm. The cytoplasm generally is clear with a fine cellular membrane. There is an ovoid nucleus with a well defined nuclear membrane. The chromatin structure is apparent. Two dark-staining nucleoli often are visible. Numerous mitotic figures are seen. Variation in the size of the individual cells led various authors to subdivide seminomas according to the size of the cells. A similarity to

spermatocytes is noted. The stroma is scanty and is made up of fine, fibrous connective tissue. The fibrous reticulum between the cells merges into larger collagenous fibers, giving the tumor its lobulated appearance in many specimens. Occasionally accumulations of lymphocytes are seen. This variation has led a number of pathologists to classify seminomas of the testis exhibiting these cells as a distinct variety of tumor. These lymphocytes are not part of the neoplastic process as such.[17,72] They are as named, lymphocytes, or adult lymphoid cells, not lymphoblasts and they[72] are not neoplastic cells. We can speculate on their origin as being the reaction to rapid growth, necrosis or infection. Thus, it is not necessary to divide seminomas of the testis into embryonal carcinoma and embryonal carcinoma with lymphoid stroma. Innes, Harvey and Dawson stated that the lymphocytes are part of the tumor, although they did not present in detail their reasons for the occasional appearance of lymphocytes.

The histopathologic characteristics of seminoma of the testis are so definite that the tumor usually can be diagnosed even when sections from metastatic deposits from any site in the body are examined microscopically.[72]

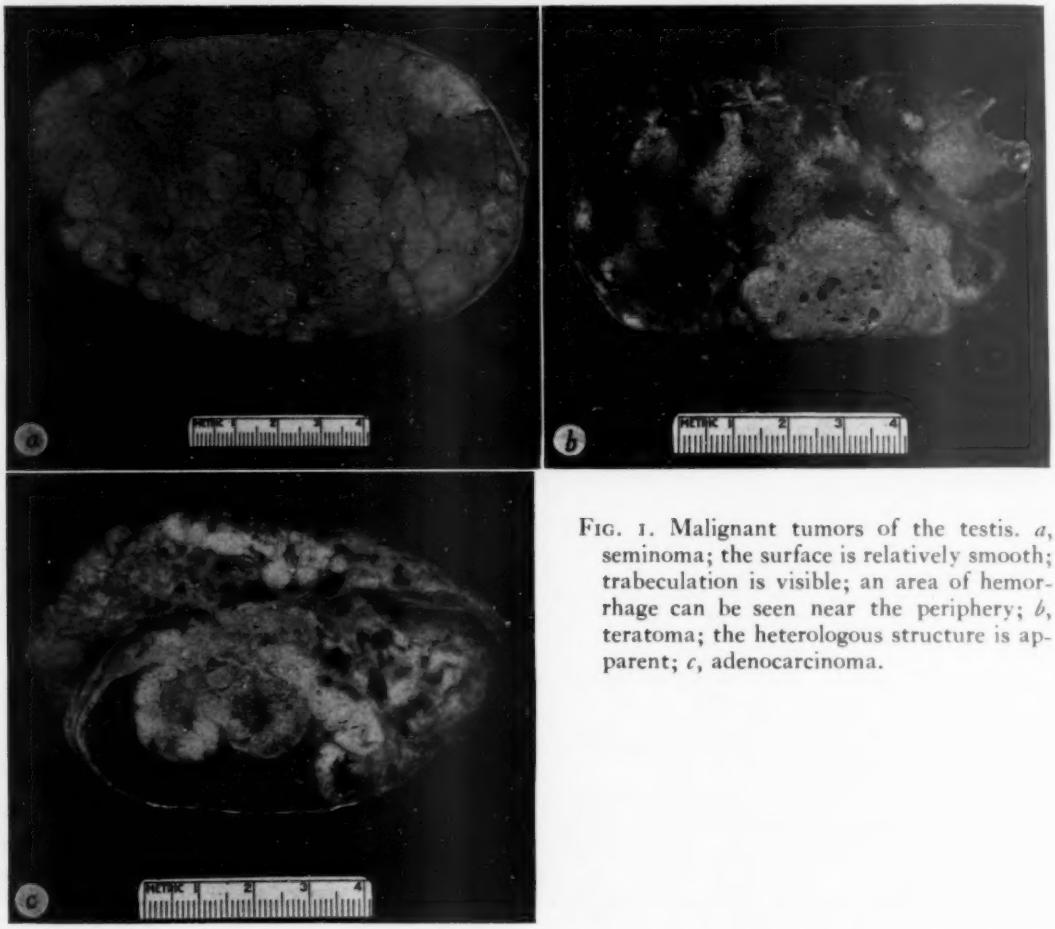


Fig. 1. Malignant tumors of the testis. *a*, seminoma; the surface is relatively smooth; trabeculation is visible; an area of hemorrhage can be seen near the periphery; *b*, teratoma; the heterologous structure is apparent; *c*, adenocarcinoma.

Figure 2, *a* and *b*, illustrates microscopic sections of seminoma of the testis. of the testis. Figure 2*a* illustrates a typical seminoma, while in Figure 2*b* a seminoma may be seen in which lymphocytes are present. These two illustrations display the variation that has led some authors to consider these as separate entities, but as explained

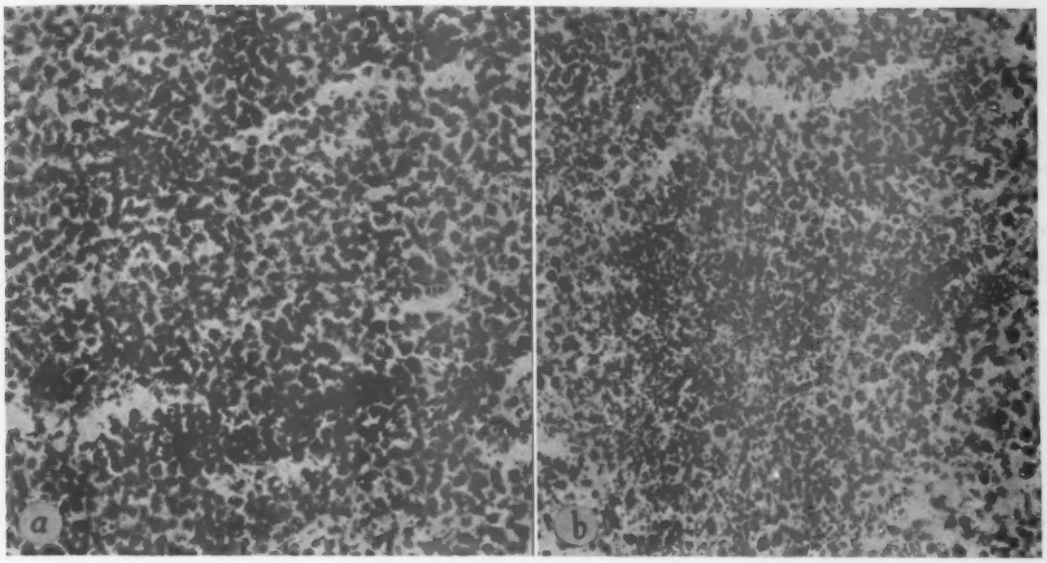


Fig. 2. Seminoma of the testis. *a*, typical; *b*, seminoma in which lymphocytes may be seen (×130).

previously, they are actually true seminomas of the testis. Figure 3*a* illustrates adenocarcinomatous elements in a teratoma. Acini are visible in this section, as well as some primitive connective tissue cells. In Figure 3*b* which illustrates an adenocarcinoma, Grade 3, of the testis, the formation of acini is the predominant feature.

Comparative Pathology. Seminomas of the testis also occur in lower animals. Innes, Harvey and Dawson presented a study of 90 cases of testicular tumors, of which 25 were in domestic animals. They found that seminoma was the most common tumor of the testis in domestic animals. Teratoid and tridermal tumors did not occur in the group of testicular tumors

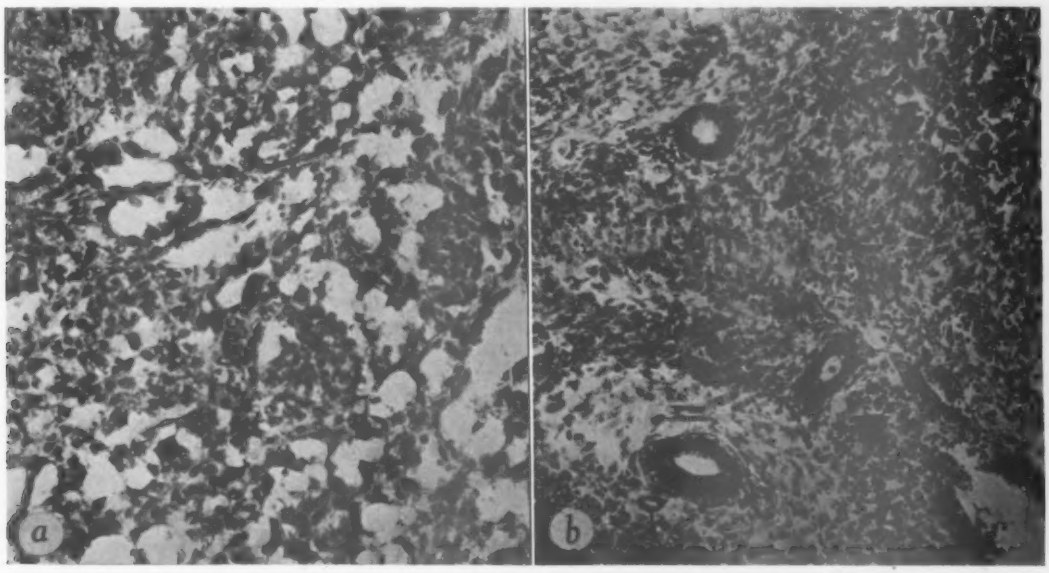


Fig. 3. *a*, teratoma of the testis. Adenocarcinomatous acini and connective tissue can be visualized (×130); *b*, adenocarcinoma Grade 3 of the testis; differentiation into acini is evident (×130).

of domestic animals they studied. Seminomas have been reported in cattle, horses, dogs, cats and roosters. Schlotthauer, McDonald and Bollman, in a study of testicular tumors of dogs, found 25 seminomas and 51 interstitial cell tumors in a group of 86 dogs. There were no teratoid tumors. These authors found that seminomas occurred in dogs at a relatively later age than they do in man. Seminomas of dogs apparently are less malignant than those of human beings and occur most frequently at about the age of ten years. Innes and co-workers presented a lucid discussion of the pathogenesis of seminomas of the testis and were of the opinion that they were derived from a cell which is younger than the spermatogonia. McDonald[73] traced the origin of seminoma of the testis to the spermatogonic series of cells, but this consideration is beyond the scope of this study.

EXPERIMENTAL PRODUCTION OF TESTICULAR TUMORS

In 1928, Michalowsky[74, 75] succeeded in producing teratomatous tumors in the testes of roosters by injection of a 5 per cent solution of zinc chloride. These tumors could be produced only during the months of the mating season, which is the period of increased sexual activity. Injections during other months did not produce tumors. In America, Bagg confirmed this work and, further, was able to produce tumors at a time other than the mating season of roosters after administration of gonadotropic substances followed by the injection of solutions of zinc chloride into the testis. Falin and Gromzewa, in 1939, reported the successful production of these tumors by the use of solutions of zinc sulfate, and Anissimova, the successful transplantation of experimentally produced zinc teratomas. Ewing,[38] after appraising the experimental production of testicular tumors, was of the opinion that these neoplasms are very different from human testicular carcinoma. Monocellular tumors have not been produced experimentally.

SEMINOMAS OF THE TESTIS AND PRODUCTION OF HORMONE

Since the literature which deals with the diagnosis and treatment of testicular tumors is so interwoven with that of the hormonal aspects of some of these tumors, no approach to the subject of roentgen treatment for seminomas of the testis would be complete without discussion of it. The fact that certain testicular tumors cause gonadotropic-like substances to be excreted in the urine also has augmented the already numerous controversial clinical and pathologic points in regard to these tumors.

Zondek[108] designated as prolan A that substance which, under proper conditions, is capable of maturing ovarian follicles of infantile small animals and as prolan B that which produces luteinization under similar conditions. In 1929, the same author[107,109] discovered the presence of a follicular ripening hormone in the urine of a man who had a testicular tumor said to be a chorio-epithelioma. The presence of a possible hormonal influence of testicular tumors manifested by gynecomastia was noted in 2 cases encountered at the Mayo Clinic prior to these publications.

Since Zondek's[107,109] reports, a veritable avalanche of literature has appeared. This literature is difficult to evaluate for several reasons: (1) there is little agreement in the pathologic classifications; (2) the mere presence of a hormone has been noted frequently, without much attention being given to either its qualitative or quantitative aspects; (3) until recently, a great deal of stress has been placed on the quantitative aspects of the hormone, if either its quality or quantity has been noted; (4) it is admitted that there is a fluctuation in the output of hormone in the urine from time to time and a systematic correlation of the times of determination with other factors, such as surgical operation and roentgen therapy, has not been made; (5) some authors express their results in terms of units other than the mouse unit, which has had more or less general acceptance as a standard; (6) the fact that deter-

minations of hormone require rather elaborate biologic apparatus has limited the application of the test, and (7) the very nature of the determination, since it is a purely biologic one, tends to give it inherent errors.

To acquaint the reader with the nomenclature we shall now define a few terms which are used in reference to the urinary hormones and their relationship to testicular tumors. European authors in particular refer to the various reactions of the ovarian follicle of the experimental or test animal after injections of urine containing these hormones as Zondek I, Zonkek II and Zondek III, by which terms they mean maturation, hemorrhage and luteinization, respectively, of the immature ovarian follicles.

The quantitative reaction of prolan A is measured in mouse units. This unit is defined as the minimal amount of urine, the extract of which, when injected into an infantile (five days old) female mouse, will produce ripening of the ovarian follicles within 100 hours.[41] The quantity of prolan A usually is expressed in mouse units per liter of urine.

Hinman and Powell[61] suggested that there are four distinct hormones which produce follicular changes in the ovaries of small animals. These are (1) the hormone of the anterior portion of the pituitary glands, (2) the anterior pituitary-like substance of pregnancy urine, (3) the hormone of testicular tumors and (4) the hormone recovered from the urine of castrates. Thus, they are not of the opinion that the anterior pituitary-like hormone of pregnancy is identical with the hormone produced by some testicular tumors.

Ferguson[41,42] has written much on the quantitative determination of prolan A in the urine of patients who have testicular tumors. He has been quoted widely on this subject, particularly with reference to the use of the quantitative test in the diagnosis of histopathologic types of testicular tumors and in the indication of their radiosensitivity. Ferguson[41] stated that there is a gradient of output of prolan A varying from 50 to 500 mouse units per liter in case of adult teratomas, from 400 to 2,000 mouse units per liter in seminomas, from 2,000 to 10,000 mouse units per liter in embryonal carcinomas of the testis with lymphoid stroma, from 10,000 to 40,000 mouse units per liter in embryonal adenocarcinomas of the testis and to more than 50,000 mouse units per liter in chorio-epitheliomas of the testis. As mentioned, embryonal carcinoma with lymphoid stroma is classified pathologically as seminoma of the testis by us. Ferguson's[41,42] observations have had a profound effect on the study of the endocrinology of testicular tumors, and the majority of authors, both American and European, seem to have accepted his statements. Since accurate and detailed determinations of the presence or absence of a gonadotropic hormone in the urine of men who have testicular tumors require elaborate biologic apparatus, reports confirming or rejecting Ferguson's work are few in number.

Grevillius questioned Ferguson's contention about the value of the quantitative test in the diagnosis of the histopathologic type of tumor, and he stated that it is not logical to suppose that a relatively small localized tumor, for example, a small, so-called chorio-epithelioma, should produce a greater output of hormone than a seminoma of the testis which has progressed to the stage where most of the abdominal cavity is filled with metastatic tumor tissue, when Ferguson admits that the amount of hormone is proportional to the amount of tumor tissue present in the body. This criticism by Grevillius also can be applied to the belief of other authors, who rely strongly on the quantitative aspects of hormones present in the urine of patients who have testicular tumors. Zondek,[109] in 1937 expressed skepticism about Ferguson's ability to ascertain the histopathologic structure from the results of the quantitative determination of prolan A.

Ferguson[42] stated that the result of the test for hormones is an accurate index of

the presence of metastasis and may be used as a guide in roentgen therapy. In 1938 Hinman and Powell[62] stated the belief that radiotherapy of metastatic masses of testicular tumors may destroy their ability to produce hormone without actually destroying the tumors. Grace reported a case in 1939 which could be classed in this group pealed for greater agreement in pathologic terminology. It would seem that the histopathologic and hormonal classification of testicular tumors as proposed by Powell,[87] a co-worker of Hinman, might be a step toward clarification. Powell subdivided the tumors usually called seminomas into three groups. These are shown in Table 1, which

TABLE I

HORMONO-HISTOLOGIC CLASSIFICATION OF TESTICULAR TUMORS (POWELL[87])

Hormono-histologic Grouping	No. of Cases	Gonadotropin M.U.L.* (Average)	Response to Irradiation	Prognosis	Result	
					Dead	Alive
I. Embryonal tumors A. Teratomata *Grade Cell Pattern*						
4 Chorionepithelioma	4	20,000 to 30,000	Fair	Poor	4	0
3 Adenocarcinoma	6	2,000 to 1,000,000	Fair	Poor	6	0
2 Differentiated (With carcinomatous elements)	8	500 to 100,000	Fair	Poor	6	2
B. Carcinomata *Grade Cell Pattern*						
4 Undifferentiated	8	1,000 to 10,000	Good	Poor	5	3
3 "éminome"	9	Below 100	Good	Fair	2	7
2 Differentiated	36	100 to 1,000	Good	Excellent	5	31
II. Non-embryonal tumors (Pathologic classification) Adult teratomata	2	Below 100		Excellent	0	2
Interstitial cell tumor	1	(Excess estrin)		Excellent	0	1

* Mouse units per liter of urine.

of phenomena, in which the fallibility of excretion of prolan A as a prognostic agent was demonstrated. Blümel reported 13 cases of testicular tumor, in which the result of the test for hormones was negative, although clinical evidence of metastasis was present.

Hinman and Powell[61, 62] have contributed much on the subject of hormones in the urine of patients who have testicular neoplasms. As lack of uniformity of pathologic classification in as obstacle to progress in this field of investigation, Hinman[62] ap- is based on a study of the results in 74 cases of testicular tumors treated by operation and irradiation and traced for from two to four years.

In Table 1, "grade" refers to ultimate prognosis. This aspect will be mentioned later. The undifferentiated embryonal carcinoma in Powell's classification, which we probably would classify as seminoma, is said by him to be a rare and malignant type of tumor composed of malignant appearing, large, bizarre-shaped cells with lymphoid stroma. The tumors designated as "*sémi-*

nome" with only a fair prognosis and the "differentiated embryonal carcinoma" with an excellent prognosis is a fine distinction, and as yet at least, not satisfactory for universal acceptance. Powell did not state his reasons for so classifying testicular tumors, but obviously he deserves a great deal of credit in making a step toward a difficult goal.

Quite in accord with the researches of Hinman and Powell,[61,62] Gerber,[48,49] in 1933, pointed out in a thorough review of the literature that seminomas are either not associated with any increase in the excretion of gonadotropic substances or with only a slight increase of the follicle maturing hormone, whereas other testicular tumors (for example, embryonal tumors with chorio-epithelioma) produce excretion of follicle maturing hormone as well as luteinizing hormone. The American literature contains little mention of the quality of the gonadotropic hormone found in the urine of patients who have testicular tumor.

At present, it appears that the quantitative test for gonadotropic substance in the urine of men who have testicular tumors is inadequate as a diagnostic aid in one main feature if the criticisms mentioned are dismissed. Bang demonstrated that the quantitative test alone is insufficient since it does not identify the type of hormone present. He revealed that it is of the utmost importance to determine the qualitative type of hormone if a division of testicular neoplasms is to be made by analysis of the hormone appearing in the urine of patients who have testicular tumors.

The classification of testicular tumors published by Hamburger, Bang and Nielson of Copenhagen, in 1935 and previously quoted herein, together with their work on analyses of hormone in the urine, is rather illuminating. To our knowledge, they are the only workers in this field who have applied both a quantitative and qualitative test for gonadotropic hormone in the urine in cases of testicular tumors in a significantly large group of patients. They subdivided gonadotropic hormones found in the urine in these cases into (1) hypophysial hormone, better signified as follicle stimulating hormone and (2) chorionic hormone, which also is called "luteinizing hormone." The hypophysial hormone, which we interpret as the actual active substance found in extract of the anterior portion of the pituitary gland, stimulates immature ovarian follicles to maturation. It causes hemorrhage and stimulates the production of corpora lutea in large numbers. The weight of the ovary of the experimental animal is increased from ten to fifteen times when urine containing this hormone in significant amounts is injected into immature mice. Normally, this hormone is present in the blood and urine in such small amounts that special methods of extraction are necessary to demonstrate it, and microscopic examination of the ovaries of the animals is necessary to study the changes produced by its injection. However, in the absence of sexual function, as in instances of castration, senility and in the climacteric, a few cubic centimeters of blood or urine containing large quantities of the hormone produces maturation only but does not produce hemorrhage or corpora lutea in the ovaries of the animal into which it is injected. Thus, these authors prefer to designate this hypophysial hormone as follicle stimulating hormone.

On the other hand, the chorionic hormone which is produced by the chorionic tissue of pregnant women, influences only a few follicles when injected into an animal; the size of these follicles is not increased more than three or four times. In pregnancy, chorionic hormone is present in such large amounts that a fraction of a cubic centimeter will produce what is known as the Aschheim-Zondek reaction, with maturation of follicles to an increased size and the production of follicular hemorrhages and luteinization. Thus, the reactions of hypophysial (anterior lobe of pituitary body) principle and the chorionic principle found in pregnancy have some similarity, but under other conditions (senility, cli-

macteric, and so forth), the hypophysial hormone is recovered from the urine or blood stream in such quantities, and its behavior is such, that since only one induces follicular maturation it is possible to separate these two gonadotropic substances in the majority of cases. Hamburger, Bang and Nielsen employed special methods of extraction and examined histologically the ovaries of animals receiving injections. They were of the opinion that there is a significant difference between the follicle stimulating hormone and chorionic hormone. This difference makes the qualitative test practical and useful although it apparently is arduous and painstaking.

Before presenting Bang's experimental results and data, which also were published in part with Hamburger and Nielsen previously, we shall quote the concluding supposition: "There are some testicular tumors which, by their presence in the organism, stimulate the hypophysis to an increase in the production of follicle maturing hormone, whereas other testicular tumors produce themselves a gonadotropic hormone that appears to be identical with the chorionic hormone found in the urine of pregnant women."

In 1938, Bang presented the results of qualitative and quantitative tests for gonadotropic hormone in the urine in 75 cases of testicular tumors (Table II). As stated, a smaller series of these were published separately under the names of Hamburger, Bang, and Nielsen.

Hamburger, Bang and Nielsen demonstrated further that in these tumors (seminomas) which produce the follicle stimulating hormone in the urine, no hormone was demonstrated in the extract of the tumor itself. On the other hand, those tumors which easily produced chorionic hormone in the urine had demonstrable quantities of hormone in even small bits of the tissue from the tumor.

Table II

BANG'S RESULTS OF ANALYSES FOR GONADOTROPIC SUBSTANCES IN THE URINE IN SEVENTY-FIVE CASES OF TESTICULAR TUMORS

Histopathologic Diagnosis	No. of Cases	Hormone not Demonstrated	Trace of Hormone	Only Follicular Hormone	Only Chorionic Hormone	Both	Radiosensitivity	Prognosis
Seminoma	42	13	4	25	0	0	Sensitive	Relatively benign
Pseudo-seminoma	2	0	0	0	2	0	Resistant	Clinically malignant
Mixed epithelioma	21	3	0	0	14	3	Resistant	Very malignant
Small cystic mixed tumor	10	4	4	4	0	0	Resistant	Very malignant

It is seen that with the use of both qualitative and quantitative tests for gonadotropic hormone, malignant testicular tumors appear to fall into two groups, namely, (1) tumors which are capable of stimulating the hypophysis to an increased production of follicle maturing hormone and (2) tumors which themselves produce a hormone that appears to be identical with the chorionic hormone found in the urine of pregnant women. Seminomas appear to belong to the former group.

It is interpreted from the analyses of Zondek[108] that the seminoma gives no increased excretion of gonadotropic hormone or only an increased excretion of follicle maturing hormone, whereas chorio-epithelioma and other malignant testicular tumors give an increase in the excretion of both the follicle maturing hormone and the luteinizing hormone.

After reviewing the American and Euro-

pean literature on gonadotropic hormones in cases of testicular tumors, our findings can be summarized as follows:

Zondek's observations on this subject and recent contributions give him the honor of having furnished the inspiration for further work in this field. In America, Ferguson's[41,42] publications have provided the impetus for investigation of these matters and they have disseminated interest in the hormones of testicular tumors. The criticisms of his work have been enumerated. Hinman and Powell[61,62] stand out because of their efforts to correlate various aspects of the subject. Their work has some agreement with other recently published researches, although it does not seem to have a finality of opinion and doubtless is not ready for universal application. Hamburger, Bang and Nielsen seem to have come closer to the solution of the question than others by their use of both qualitative and quantitative hormonal tests. As a result of their work, practically the entire literature on testicular tumors in the past few years favors the use of some form of bioassay of hormones in cases of testicular tumors.

The performance of proper biologic determination of hormones entails an expense which is beyond the reach of all but a few centers; to indicate this, the incidence of testicular tumors and the exacting conditions under which the tests must be performed have only to be recalled. Magath[70,71] noted the requirements for the test and mentioned the difficulties encountered in it, together with the cost of such a procedure. Few centers have large colonies of mice available from which the test and control animals can be selected. A probable solution might be the development of a chemical test for the gonadotropic hormones in the urine of men who have testicular tumors. Efforts have been made in this direction, which reveal some promising correlative results.[80]

A number of side reactions complicates these tests, over and above the shortcomings of any biologic test. As applied to tumefactions of the testis, misleading positive results have been recorded by Owen and Cutler in cases of granuloma of the testis, epididymitis and testicular cysts.

The prognostic significance of the determination as regards testicular tumors of all types is at best questionable. Its value as an index of the presence of metastasis may be valid, but this feature also has been criticized.

As a group, seminomas of the testis do not produce any hormone which can be demonstrated by present methods, or if they do produce a hormone it is the follicle maturing type only. A review of the cases of seminoma made by Grevillius and by Bang in which an increased amount of hormone was found in the urine revealed that the majority of the tumors were not pure seminomas.

We have not found reports which indicate whether the two types of seminomas (the type in which there is no gonadotropic hormone in the urine and that in which there is only a small amount of the follicle maturing hormone as mentioned by Powell) display a difference in radiosensitivity that is sufficiently convincing to be conclusive.

In the light of present knowledge we cannot subscribe to the exclusive application of the test in the differential diagnosis of seminomas since the definite diagnosis is and can be made microscopically from histologic sections and since a certain group of seminomas produce no hormone.

The exact position of the test for hormones is undecided at present. Possibly, some important feature of the determination has yet to be improved. Dean,[27] in 1939, warned against overenthusiasm for the test for gonadotropic substances in the urine of patients who have testicular tumors. He stated: "The Aschheim-Zondek test [that is, the determinations for prolan A, mouse test and test for gonadotropic hormones in the urine in cases of testicular tumors] in my opinion, is an unsafe basis for clinical procedures at the present time."

Our experience with determinations of

gonadotropic substances as applied to seminomas and the value of such tests in the radiotherapy of seminomas has been limited and, for the present, we can draw no conclusions. Since this material was prepared for publication Ferris summarized his investigations of the hormonal relationships of testicular tumors as follows:

Tumors of the testis are rare, and almost all are malignant. Two types of tumor, the seminoma and teratoma, comprise almost all malignant tumors of the testis.

All malignant tumors of the testis cause excretion of excessive amounts of gonadotropic hormone in the urine. Twenty rat units per liter of urine is the dividing point between normal and excessive amounts. The test must be quantitative and the best technic is that of Frank. The best routine on the first analysis is to test for 25, 40 and 66 rat units of hormone per liter of urine.

CLINICAL FEATURES OF SEMINOMAS OF THE TESTIS

The purely objective clinical characteristics in 103 proved cases of seminomas of the testis have been reviewed by us to determine if data in the history of clinical findings in a proved case of seminoma of the testis will enable an accurate clinical diagnosis of the condition. We have purposely omitted an analysis of symptoms, as obviously symptoms are subjective phenomena in which personal, and perhaps erroneous, interpretation may be drawn. We likewise have not considered in detail the duration of seminomas as compared with other testicular tumors because it is our belief that the duration of testicular tumors, as stated by the patient, often is grossly erroneous.

Tumor Mass. In the majority of cases, the obvious presenting sign was a tumor mass associated with the testis. The presence of a mass in its earlier stages of development was not noted among those patients who had abdominal testes; in a small proportion of cases reviewed by others it has been noted that evidence of metastasis was present before the tumor in the testis was detected. This was noted in 1 case in our series of 103 seminomas of the testis. The patient had complained of symptoms referable to a large mass in the right upper quadrant of the abdomen for six months; the primary testicular tumor was unknown to him. It was discovered in the course of a physical examination and was only 1 cm. in diameter.

Age. It is generally stated that seminomas of the testis occur most frequently during the years of greatest sexual potency. As can be seen in Figure 4, the greatest incidence in our cases was in the fourth decade, in which 39 per cent of the tumors occurred; 24 per cent were found in the fifth decade and 24 per cent in the third. On comparing this age distribution with that in representative groups of Chevassu[24] and Grevillius our findings are in agreement.

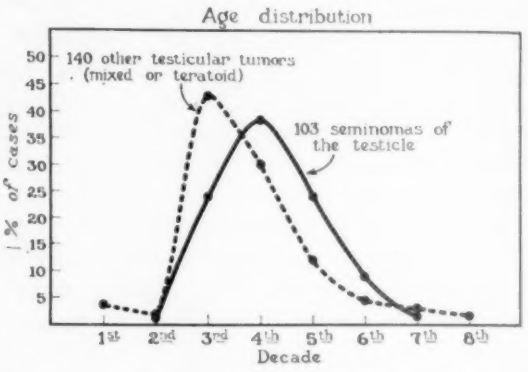


Fig. 4. Age distribution by decades of 103 seminomas of the testis and 140 other testicular tumors.

Seminomas of the testis have a relatively later peak of maximal incidence, and occur most often approximately a decade later than other malignant testicular tumors of the more common varieties. To illustrate this, we have plotted in the accompanying graph (Fig. 4), in addition to the number of seminomas in our series of 103 cases, a selected group of 140 cases of testicular tumors which were not seminomas, chosen from the reports of Gordon-Taylor and Till, Chevassu,[20] Deitermann,[28] Desjardins,[29] and Grevillius. Since we had some difficulty in selecting these mixed or teratomatous

tumors (illustrating the confusion in pathologic classifications and the influence of certain teachings in America), we were obliged, for the most part, to consult European reports. These cases were selected as representative "mixed" or "teratoid" tumors, in that the percentile incidence of seminomas in the various series from which they were selected was more or less constant and consistent with ours, and so the remaining tumors of the mixed or teratoid variety most probably also conform to the microscopic criteria to which we adhere. In other words, we are certain our 103 cases are cases of seminoma; and we are reasonably certain that the 140 cases listed and collected from the literature are cases which display other testicular tumors, notably of the mixed or teratoid type, largely because many authors separate seminomas from other tumors and because their incidence is probably correct.

It is seen, then, that seminomas of the testis occur later in life than other varieties of testicular tumors, and in this respect they are different from other testicular neoplasms. Smith, Dresser and Mintz found a similar occurrence, but their pathologic classification does not agree with ours.

Side Involved. In 52 of our 103 cases, seminomas were in the right testis and in 51 in the left. Dean's[27] statement that involvement of the right testis by tumor is more common than the left is justified when the relationship of cryptorchidism to tumor of the testis is studied. Peirson,[82] in 1932, collected from the literature 46 cases of bilateral testicular tumors of all types and reported a case of his own. Simultaneous bilateral testicular tumors rarely occur, according to Peirson,[82] whose case was of this type. Lewis and Priestley reported 2 additional cases of bilateral testicular tumors in 1938; in 1 of these the tumors appeared simultaneously, as far as was known. In each case, both tumors were seminomas. In their review, they found 3 additional reports of cases of bilateral testicular tumors which had been published since Peirson's[82] report.

Cryptorchidism. It generally is stated that the not fully descended testis is more prone to undergo neoplastic change. Cryptorchidism is more common on the right than on the left side. Smith[99] stated that 50 per cent of undescended testes were on the right, 36 per cent on the left and 14 per cent were bilateral. Hence, it is apparent that in large series of cases there should be more tumors of all types involving the right testis than the left. This, however, did not occur in our group of seminomas.

Rea[92] indicated that the abnormally placed testis has 220 times the possibility of becoming malignant that the normal scrotal organ has. Hinman and Benteen[60] stated the figure as 20 rather than 220. We are inclined to agree with the latter authors since their statistical method seems subject to less error than does Rea's deduction. Chevassu[20] found cryptorchidism in 11.7 per cent of 128 cases of testicular tumors. Dean[27] placed the figure at 14.29 per cent and Higgins and Buchert at 8.4 per cent. An average incidence of cryptorchidism in 1,787 cases of testicular tumors collected from the literature by Grevillius was 13.3 per cent; Rubaschow found the figure to be 14 per cent from a survey of the reports of twenty authors. Schlotthauer, McDonald and Bollman, in a small series of dogs, found an increased number of seminomas in dogs which had undescended testes.

In an agreement with Ewing,[37] and without taking into consideration the traumatic origin of malignancy in ectopic testes, it seems to us that some biologic inferiority resulting in, or from, cryptorchidism might be associated with formation of tumor in these cases. In fact, certain histopathologic and, perhaps, physiologic differences have been noted by some authors in those tumors developing in the ectopic organ.[89] In 9 (8.7 per cent) of our 103 proved cases of seminomas of the testis, seminoma of an undescended testis was present; in 2 others the opposite testis was undescended.

Hydrocele. Hydrocele was found either clinically or at operation in 20 (19.4 per cent) of the 103 cases. Higgins found

hydrocele in 18.1 per cent of the cases in his group, and Grevillius in 20 per cent of all cases of testicular tumors. That a sympathetic hydrocele may develop with the distortion of normal relationships by neoplasm is possible. The formation of hydrocele in certain cases undoubtedly is due to the reaction of the serosal surfaces of the tunics when invaded by tumor; the mechanism is comparable to that of pleural effusion in cases of pulmonary carcinoma.

Varicocele. Varicocele was present in 2 of our cases. It was noted in the gross pathologic description of seminomas that the surface of the tumor occasionally displayed a network of dilated veins. If we accept the presumption that varicocele might be caused by interference with venous return from the testis, or by a relative increase of arterial flow, then the presence of a tumor in some cases could result in some degree of varicocele.

Consistence of Tumor. Ordinarily, seminomas are described as elastic and only rarely as firm or hard. Although we realized that consistence is largely a matter of judgment on the part of the examiner, we found enough variation from the classic descriptions to note it.

In contrast to the usual description, the tumors were described as hard in 48 of the 103 cases, as firm in 23 and as cystic in 10. Fluctuation was described in 2 cases, and 1 tumor was said to be soft. Since there is a wide variation in both actual consistence and in the examiner's personal interpretation of consistence it alone cannot be considered to be diagnostic and thus it would appear that on that basis a diagnosis of seminoma could not be made.

Fever. A slight elevation of body temperature to between 99 and 100° F. (37.2 and 37.7° C.), was noted in 14 of our cases. Nine of these patients had demonstrable or presumptive metastatic lesions in the abdomen.

Family History. None of the patients in our series gave a family history of testicular tumor. Raven reported testicular tumors in brothers; 1 tumor was a seminoma; the other was not diagnosed pathologically. Lownes and Leberman, in 1939 reported testicular tumors in brothers but the diagnosis in 1 case was questionable since adenocarcinoma of the prostate gland also was present; tissue removed from the testis revealed well differentiated adenocarcinomatous elements, which might not have been testicular in origin.

Trauma. A history of trauma may frequently be elicited in cases of testicular tumor. Various authors, including Cairns, Dean,[27] Smith and associates,[100] Gordon-Taylor and Till, and Higgins and Buchert, noted this factor in from 10 to 30 per cent of their cases of testicular tumors of all types. Collins recently placed the figure much higher and stated that in 68.8 per cent of 51 cases of testicular tumors a history of trauma was present. In our series of 103 proved cases of seminoma of the testis, in 21 (20.3 per cent) there was a history of direct injury to the testis, before the occurrence of mass. The fact that the testis is an exposed organ and that even trivial injuries produce severe pain, and the fact that these incidents are remembered by the patient oftener than are corresponding degrees of trauma elsewhere in the body, may contribute to the comparatively large incidence of trauma which has been reported. Since most active men, particularly those in the less sedentary occupations, often receive testicular injuries, too much significance should not be attached to the alleged rôle of trauma.

Ewing[37] laid down a number of strict conditions to be met before a relationship between trauma and malignancy can be accepted. He drew attention to the fact that often trauma incident to an inguinal testis is the ascribed cause of malignant change in such an ectopic organ, but he did not subscribe to this belief. If the criteria of Ewing[37] were satisfied in each case of testicular tumor in which a history of trauma is present, the percentage of significant trauma probably would be considerably lower than usually is given.

Infection. A history of gonorrheal ure-

thritis was related by 18 of our 103 patients. One of these 18 patients had had complicating epididymitis. Four had had mumps. Of these, 3 had had mumps orchitis in the testis involved. One patient had had a previously atrophied testis and another a nonspecific type of inflammation after an attempted needling of a suspected hydrocele two years before registration at the Clinic. In all, 6 patients gave a history of previous inflammatory lesions of the testis or epididymis. Thus, inflammation obviously is not an important factor in the etiology of seminoma.

Syphilis. A history of arrested syphilis was obtained in 1 case and a weakly positive result of the precipitation test for that disease was found in another.

Other Data. Other findings were present in the more advanced cases, but these were less frequent. Cachexia, loss of weight, pallor, anorexia and exhaustion were noted. The breasts were swollen in 2 cases, in one of which secretion from the nipple was noted.

Duration of Symptoms. An analysis of the duration of symptoms was not made except to note that this period was extremely variable. It is likely that the average duration of the disease is shorter in the cases encountered in a private urologic practice or in a large city dispensary where attention is available earlier than in our cases.

Gordon-Taylor and Till divided seminomas into four groups according to the duration of symptoms, namely (1) the slowly growing, painless, insidious type of "average" seminoma; (2) the rapidly growing "hurricane" type,* which is fulminating in a matter of weeks; sometimes this type presents acute preoperative symptoms not unlike orchitis; (3) the slowly growing type, which persists for years with no apparent change, and (4) the type in which the primary tumor is not apparent but in which metastatic lesions cause symptoms. In studying the cases in which the disease allegedly is of short duration, the accuracy of the patient's memory may be questioned or the patient may not have been aware of the presence of a long standing tumor with mild symptoms. On the other hand, that some benign tumefaction was present to give a so-called long duration is a tenable supposition. At any rate, our experience agrees with Gordon-Taylor and Till's duration of the clinical types

In 14 (13.6 per cent) of the 103 cases of seminoma of the testis, symptoms of the disease had been present for four or more years. In 2 of these the disease had been present for an extremely long time, sixteen years in one case and twenty years in the other. There were 13 cases in which symptoms had been present for less than eight weeks. No attempt is made in this report to analyze statistically the duration of cases either with or without metastasis, other than to mention that there seemed to be no rule or regularity about the duration of symptoms, for, in cases in which metastasis was not demonstrated evidence of a tumor had been present for relatively long periods of time (six and seven years). Likewise, in a number of cases in which metastasis was demonstrated on first examination at the Clinic the primary tumor had been known to be present only a few weeks. The division of cases into clinical types, according to Gordon-Taylor and Till, seems to have a sound foundation in consideration of the duration, and it reveals that in most cases of seminoma of the testis no rule can be followed in attempting to correlate the duration of the symptoms with the diagnosis of the lesion.

METASTASIS FROM SEMINOMAS OF THE TESTIS

Because of the extreme importance of the manifestations of metastatic deposits from testicular tumors, particularly seminomas of the testis, in the management of these cases we shall consider this aspect carefully. To this point, we have omitted

* One of us (L.A.N.) recently observed a hurricane type of seminoma in the case of a boy sixteen years of age, whose death occurred one month after onset of a generalized cutaneous "rash." At necropsy extensive metastasis to the organs and skin was found; the primary tumor was verified but had not become manifest during life.

purposely any reference to this phase of the subject in order to discuss at this time the related anatomic and pathologic fundamentals so necessary before a thorough understanding of the clinical phenomena of metastasis from these tumors can be established.

From the standpoint of roentgen treatment these fundamental relationships

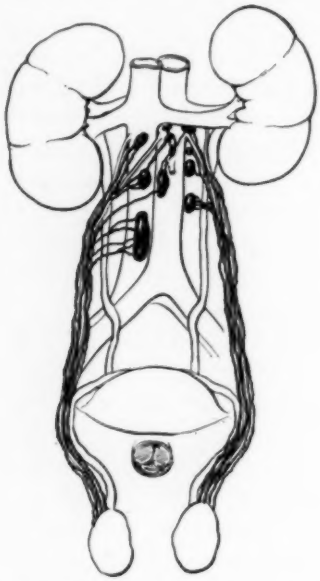


Fig. 5. Lymphatics of the testis. (Adapted from Rouvière,[31] with permission of Dr. M. J. Tobias.)

should form the basis and guide for proper treatment of seminomas of the testis.

Related Anatomic Features. Rouvière pointed out that the lymph capillaries of the human testis originate in a compact network around the seminiferous tubules in the lobules of that organ, from which they pass into the interlobular septa. The majority of these small lymph vessels leave the septa to reach the tunica albuginea and follow the surfaces of the testis toward the posterosuperior border of the organ. A few small lymph vessels pass by way of the mediastinum testis to arrive at the same point, where they eventually join, ascend and anastomose along the blood vessels of the spermatic cord (Fig. 5).

These collecting lymphatic trunks are placed more superficially than the blood vessels in the cord, and they vary in number from four to eight. These increase by division caudally. The testicular collecting trunks accompany the internal spermatic artery and vein and begin to separate from the blood vessels near the point where the spermatic blood vessels cross the ureter. The collecting trunks turn medially by describing a curve, concave below, or by bending sharply and following a more or less transverse or oblique course toward the abdomino-aortic nodes into which they empty. The nodal connections of these lymphatics differ on each side of the midline of the body.

The collecting trunks on the right side run to the abdomino-aortic nodes, which lie near the aorta from the level of the renal vein to the bifurcation of the aorta. Among these lymph nodes are those which receive the testicular collecting vessels more frequently than others. In this manner, two or three precaval nodes always receive two, and sometimes three, collecting vessels. The lowest precaval node, placed opposite the bifurcation of the aorta, almost always receives one of the collecting trunks. The preaortic nodes receive one or two lymph trunks in from a third to a half of cases. Less frequently, one of the collecting trunks terminates in a laterocaval node situated in the angle formed by the renal vein and inferior vena cava.

On the left side, the collecting trunks also drain into the abdomino-aortic nodes. All the collecting trunks on the left run to the lateral aortic nodes below the renal pedicle and usually end in the superior nodes of this group, but some may end in a node at the level of the aortic bifurcation. In a third of the cases, all the collecting trunks do not terminate in the lateral aortic nodes; one, two or three of these terminate in the preaortic nodes.

There are connections between the testicular lymphatics and the iliac lymph nodes. The abdomino-aortic nodes are not the only direct recipients of the lymphatics of the testis. Some observers have found a lymphatic vessel terminating in the iliac

nodes. It ascends along the ductus deferens and accompanies this structure to the vesical peritoneum, from which point it deviates outward, backward and upward to terminate in an external iliac node placed on the external iliac vein in front of the point where the latter is crossed by the ureter. This lymphatic trunk apparently is associated closely with a trunk from the epididymis. The majority of trunks from this latter structure accompany the internal spermatic artery; some accompany the deferential or even the external spermatic artery and end in the external iliac or hypogastric nodes. These connections of the lymphatics of the testes and the external iliac nodes occur only exceptionally.

The abdomino-aortic nodes are composed of an aggregate of from forty to fifty nodes, and are divided into four main groups; these are the pre-aortic, the right and left lateral aortic and the retro-aortic lymph nodes. The pre-aortic nodes receive, among others, the collecting lymphatic trunks of the testis, as do the lateral aortic lymph nodes. All the abdomino-aortic nodes anastomose with each other, forming a dense plexus of lymphatic vessels around the prevertebral blood vessels. From this dense plexus arise the lumbar lymph trunks.

This group of nodes, together with the anastomotic plexus, forms the first zone of defense or the first zone of involvement of lymph nodes in cases of spread from tumors of the testis.

Two lumbar lymph trunks usually are present, a right and a left. The left arises from a number of roots from the lateral aortic and retro-aortic nodes. The right arises from the interaorticovenous, retrocaval and lateral caval nodes. The left usually is larger than the right. These trunks are tortuous and pass through the aortic hiatus of the diaphragm to ascend and converge to join the thoracic duct.

The thoracic duct is the lymph collecting trunk for the infradiaphragmatic portion of the body, except for a few lymphatics from the liver and those from the upper portion of the anterior abdominal wall. It extends from the lumbar nodes inferiorly to empty into the left jugular vein at the junction of the subclavian vein with the internal jugular vein. It ascends in front of the vertebral column, running to the right of the aorta and traversing the superior aperture of the thorax on the left. In the thorax, the duct receives intercostal and juxtavertebral lymphatic vessels. Finally, it terminates into the internal jugular vein or in one or more of the several variations of the termination of this portion of the lymphatic system into the general venous circulation.

The purpose of this review of the anatomy of the lymphatics of the testis will be even more apparent when the clinical manifestations of metastatic lesions are considered.

Incidence and Site of Involvement. Metastasis was noted at the time of the first examination at the Clinic in 47 of the 103 cases. The most common site of secondary involvement was in the abdomino-aortic (retroperitoneal) group of lymph nodes, and this site was involved in 25 (24.2 per cent) of the 103 proved cases of seminoma of the testis. The mass usually was palpable in the epigastrium, predominantly on the side of testicular involvement, but often it crossed the midline of the abdomen.

Involvement of the inguinal nodes by metastatic lesions at the time of the first examination at the Clinic was next in frequency; this occurred in 24 cases (23.3 per cent). Spread to this site usually is a late phenomenon, as has been pointed out by Desjardins,[33] and indicates perforation of the capsule of the testis by the seminoma, or possibly by direct involvement, since Rouvière has mentioned that there are some uncommon lymphatic connections between the lymphatics of the testis and the lymph nodes of the external iliac group. This latter supposition is not as well grounded as the knowledge of the lymphatic drainage paths of the parietal tunics and scrotum, which structures drain into the external iliac group of nodes in the groins.

The lungs were involved in 2 of the 103 cases at the time of the first examination. With the exception of this site of metastasis, which was demonstrated by roentgenograms of the thorax, all of the metastatic findings were demonstrated by physical examination. Secondary involvement of the lungs is reported to be much more frequent than we found it. Smith, Dresser and Mintz found pulmonary involvement in 23 per cent of their cases. Young and Davis[106] stated that the presence of multiple tumor nodules in the lungs of a man in the prime of life should be considered as evidence of testicular tumor until proved otherwise. However, Desjardins and one of us (E.T.L.[66]) found that in their cases pulmonary metastasis was a relatively late and rare phenomenon.

Evidence of metastasis in approximately half of our cases of seminoma indicates that the tumor is a widely metastasizing neoplasm. In general, this observation would indicate that treatment was instituted late in the course of the disease. However, in 75 per cent of the cases of testicular tumors studied by Dean[26] in 1935, evidence of metastasis was present when radiotherapy was begun, and the same author[27] recently mentioned 39 cases which were encountered in the first three months of the disease; metastasis had occurred in 67 per cent of these. In this group the so-called cases of fulminating tumor were excluded. For obvious reasons, it is difficult to evaluate an author's data on metastasis and to compare the figures of various writers. Most of them state that the incidence of metastasis is high. In other words, metastasis from seminomas of the testis seems to occur early in the course of the disease.

MacKenzie and Ratner, in a study of metastasis from tumors of the testis, mentioned that secondary lesions from testicular tumors of all types occur in the lungs, pleura, liver, spleen, kidneys, suprarenal glands, brain, heart, skull, spinal column and cord and pelvis, in addition to the sites already mentioned. According to Desjardins,[34] these loci are relatively uncommon, except perhaps the lungs, and metastasis to them occurs either infrequently or late in the course of the disease. MacKenzie and Ratner stated that spread may take place directly by way of the blood stream, by penetration of the pampiniform plexus of veins, without detectable lymphatic involvement. The spread of seminomas of the testis, like that of most malignant epithelial tumors, is generally by way of the lymphatics and, as has been noted, usually occurs early in the course of the disease. It is more than likely that spread by way of the blood stream originates in spread through the primary lymphatics by way of the thoracic duct, since, in our own experience, involvement of the primary group of lymph nodes in the retroperitoneal space was by far the most common metastatic manifestation. Metastasis to the rarer loci was accompanied by involvement of the primary lymph nodes.

Since, for all practical clinical purposes, the earliest and most common site of metastasis from seminoma of the testis is in the retroperitoneal lymph nodes, and since metastatic involvement of other parts of the body takes place after retroperitoneal metastasis, and because of the importance of abdominal metastasis in regard to treatment and prognosis, we shall sum up the physical signs and symptoms of retroperitoneal metastasis from a recent paper by Desjardins.[33]

Signs and Symptoms. As the pathologic manifestations of metastasis from seminomas become familiar and these changes can be visualized, the explanation of the symptoms produced becomes lucid. Desjardins[33] stated that retroperitoneal lymphadenopathy often produces pain in the back which usually is dull and aching in character and is regarded by the patient as "lumbago." However, the pain often extends to the lower extremities like sciatica. Desjardins stated that the usual differential diagnostic methods for organic nervous or spinal diseases offer no clue to the nature

of the disease. The pain is due to the pressure of enlarged lymph nodes on sensory nerves in the abdomen, probably branches of the lumbosacral plexus. Abdominal pain is often present and varies in type with the location and the amount of involvement of the lymph nodes. Constipation often accompanies this condition. Bloating and belching, associated with a feeling of fullness in the epigastrium, are common symptoms. Epigastric metastatic deposits may produce mechanical interference with the function of the upper gastrointestinal tract, and symptoms simulating cancer of the gastrointestinal tract are not infrequent. Occasionally, symptoms referable to the abdominal viscera may become so sudden and spectacular as to simulate an acute surgical emergency.

Early metastatic lesions produce few and vague physical signs. As the lymph nodes become larger, they form a mass, usually on the same side of the abdomen as the involved testis. In cases of seminoma, the usual location of the metastatic mass is in the epigastrium. If a definite mass cannot be palpated because it is too small, only deep resistance in the abdomen may be found. Desjardins[33] pointed out this fact and emphasized that pressure by the examiner's hand on this deep and vague abdominal resistance elicits definite tenderness which is not found after similar pressure on a normal abdomen. A definite, palpable mass may be smooth or nodular and usually is firm and immobile. If examination is not made carefully, the metastatic tumor may be mistaken for enlargement of one of the parenchymatous organs. In addition, Desjardins[33] stressed the importance of having the patient in the proper position in order to examine the abdomen for metastatic growths. The patient should be recumbent with his head slightly flexed on a pillow, his thighs should be slightly flexed on the trunk, and the upper extremities should be at rest along the trunk. He should breathe through his mouth to help relax the anterior abdominal wall. Mere casual palpation is not sufficient. Careful, orderly, systematic methods of examination, after satisfying the conditions as to the position of the patient, will enable earlier and smaller abdominal lesions to be demonstrated, which might be missed by a less careful examination.

DIFFERENTIAL DIAGNOSIS OF TESTICULAR TUMORS

The differential diagnosis of tumor of the testis usually is not difficult. It has been suggested by Oberndorfer that any noninflammatory tumefaction of the testis should be considered as a malignant testicular neoplasm until proved otherwise. The common error is that tumor is not thought of, and the lesion is considered inflammatory or otherwise benign. For a more complete presentation of the matter of differential diagnosis, reference to the standard urologic textbooks is desirable, but for purposes of continuity we shall outline several conditions with which tumors of the testis may be confused.

It has been pointed out, notably by Dean[27] and Belt, that in cases of hydrocele, as contrasted to tumor, the penis is partially obscured by surrounding soft tissues, whereas in tumefactions of the testis there is a more or less definite line of demarcation of the swelling. It should be recalled that every fifth case of seminoma of the testis is associated with hydrocele. Herman condemned the practice of promiscuous needling of hydroceles as a diagnostic procedure and insisted that hydroceles should be tapped only after their presence is confirmed by transillumination.

Spermatocele is less common than hydrocele, but presents similar difficulties in differential diagnosis. Hematocele generally presupposes a history of trauma, but Dean[27] noted that bloody fluid in a hydrocele often indicates a tumor. Tuberculosis usually involves the epididymis rather than the testis; other foci of tuberculosis are usually present and demonstrable.

Gumma of the testis is rare. The finding

of syphilitic manifestations elsewhere in the body, or a positive result of a serologic test for syphilis may help to distinguish this condition from malignant tumor of the testis, although a positive result does not exclude tumor, since tumor and syphilis may exist together. By the same token, any of the other differential possibilities may be present with tumor.

Scrotal hernia may be confusing, but it should not be too difficult to distinguish from tumor of the testis.

Scar tissue in the scrotum, buboes mistakenly diagnosed, and other lesions of the groin and scrotum, also should be listed in the differential diagnosis.

Sometimes exact diagnosis is possible only after surgical exploration. Although the clinical material is presented here in only the briefest possible form, the confusing clinical pictures ensuing from metastasis to various parts of the body, particularly the retroperitoneal region, must be remembered. A diagnosis of hepatomegaly, splenomegaly, gallstones, hypernephroma or an acute gastrointestinal condition requiring emergency treatment or other conditions may be made while the existence of metastatic testicular tumor is not recognized. This is particularly true in the cases in which minimal primary lesions are demonstrated.

BIOPSY IN THE DIAGNOSIS OF SEMINOMA OF THE TESTIS

Dean[26] advised the use of needle biopsy prior to preoperative irradiation. This method was not used in any of our cases. Broders thinks that, with the needle, not enough tissue is obtained to establish an accurate diagnosis.

As far as we know, little about biopsy is mentioned by the various authors who have contributed to the literature of testicular tumors. It is our opinion, as gathered from the writings of Hinman,[62] that he favored immediate removal of the entire involved testis rather than the use of a small bit of tissue for histopathologic examination.

According to Priestley, it has been the practice of the surgeons who performed operations in these 103 proved cases of seminoma of the testis to remove the entire primary tumor including the testis, without preliminary biopsy.

TREATMENT OF SEMINOMA OF THE TESTIS

General Plan. In the development of treatment for seminomas, as for other testicular tumors, the most obvious and easiest method of therapeutic attack was simple surgical ablation of the involved testis. The fact that this procedure was not enough to effect more than a relatively small percentage of cures became evident soon after serious attention began to be paid to these tumors. Kober, in 1899, found that there was a three year survival rate in only 20 per cent of 114 cases of testicular tumors of all types which he collected from the literature. Only a third of the 47 patients who had seminoma and whose cases were reported by Chevassu[21] in 1910, survived four years. Reports of other authors are in general agreement. Tanner, in the United States, studied 600 cases of testicular tumors of all types and reported in 1922 a four year survival rate of only 6 per cent after simple orchidectomy. Wasterlain, after reviewing a number of cases of testicular tumors of all types from the European literature, stated in 1932 that only 6 per cent of the patients lived two years after simple orchidectomy. Dean pointed out that this figure is approximately the same as the incidence of adult teratomas in tumors of all types found in the testis. The adult teratoma accounts for about 7 per cent of all testicular tumors and behaves as a benign growth with malignant potentialities. From the foregoing, it can be concluded that simple castration as a curative measure has been found wanting.

The so-called radical operation for testicular tumors should be considered in surgical treatment of seminoma of the testis. This involves essentially the removal of the primary tumor, together with its tributary lymph nodes as far as the retroperitoneal space, and is a rather formidable operation. Although Chevassu[21] stated that Kocher, in 1882, operated on a patient who

had a metastatic lesion in the abdominal cavity from a testicular tumor with some degree of success, the first attempt at complete radical removal of metastatically involved lymph nodes in the retroperitoneal space was made by Roberts in 1902; however, his patient died. Grégoire usually is credited with the first successful radical operation in 1905. The names of Chevassu[20,21] and Hinman[59] usually are associated with development of the radical operation.

In the operation as described by Hinman,[59] an anterior approach to the retroperitoneal lymphatics usually is made extraperitoneally, and the abdomen is entered latero-anteriorly on the side involved. The peritoneum is stripped and reflected, and the contents of the abdominal cavity are retracted in order to expose the retroperitoneal space from the level of the bladder to the renal pedicle. The primary and anastomotic lymphatics draining the testis are thus exposed and resected; the involved testis usually is removed first.

Radiotherapy of testicular tumors has slowly narrowed the indications for radical operation. In fact, from the writings of Hinman[58,59,62] we are able to gather that radical operation does not now enter into the treatment of seminomas of the testis to any great extent. At present it seems to be reserved only for those patients who have malignant testicular tumors, who are in good physical condition, without evidence of metastasis, and who have a radioresistant tumor, either with or without hormone in the urine. This information is obtained from the results of physical examination, hormonal tests and the hispathologic examination of the excised testis before radical operation is decided on. We have not been able to determine whether the difference in radiosensitivity of the tumor designated by Powell as "séminome," as contrasted with his "differentiated embryonal carcinoma," is sufficient to place the former tumor in the group suitable for radical operation. Our impression is that Hinman and Powell do not recommend radical operation for these tumors, certainly not as the only therapeutic procedure, since the majority of a group of patients subjected to radical operation received roentgen therapy in addition to the radical operation.[58]

If, from the writings of Hinman and Powell, we admit the possibility that some seminomas may be less radiosensitive than others and are better surgical than irradiation risks, we are still sufficiently satisfied to state that in our opinion all tumors which we designate as seminomas should receive roentgen therapy after simple primary orchidectomy. The problem, of course, is to determine radiosensitivity before metastasis appears, so that radical operation may be performed within the true indications for it as laid down by Hinman.[59] We have already stated that, as yet, the biologic hormonal tests do not offer definite or conclusive information about the radiosensitivity of testicular tumors that is practical enough for everyday clinical use. To estimate radiosensitivity from the histopathologic appearance of the tumor[59] is, at best, uncertain, but we do know that seminomas certainly have a characteristic microscopic picture and that seminomas are radiosensitive.

The fact remains that, in spite of some variation in the radiosensitivity of seminomas, the other uncertainty of attempting to determine nonradiosensitivity by biologic methods, together with the hazards of other types of treatment, such as the radical operation, are much more serious than the possible chance that the seminoma may prove more resistant than usual. The proponents of the radical operation are to be congratulated on pioneering and perfecting a most difficult type of surgical technique. We cannot discuss it exhaustively for we have not had any experience with it.

MacKenzie and Ratner, who studied metastasis from testicular tumors, cast doubt as to whether the radical operation is anatomically feasible. They stated:

> In 1910, Jamieson and Dobson, after extensive studies of the lymphatics of the testis, demonstrated that the arrangement of these lym-

phatics is such that the complete removal is exceedingly difficult and dangerous, if not impracticable. It is this anatomy of the lymphatic drainage that has convinced several surgeons of the futility of the radical operation for teratoma of the testis. These men claim that if a radical removal of the glands is undertaken, it should include the lymph nodes beyond the renal region as well, but that procedure is of course impossible.

The use of mixed toxins of *Streptococcus pyogenes* and *Serratia marcescens*, as advocated by Coley, seems to have fallen into more or less general disuse.

At present, the general opinion is that there is only one type of treatment for probable or actual metastatic lesions after surgical removal of the involved testis, namely, radiotherapy, which is perhaps carried out best by the use of roentgen rays.

In Desjardins'[31] classification of the order of radiosensitivity of various body cells and tissues, the basal epithelial cells of the testis and ovary are considered highly sensitive. In Desjardins'[30] classification of the order of sensitivity of tumors to roentgen rays and radium, tumors of the seminal epithelium also are found to be highly radiosensitive. Paterson grouped seminomas with the definitely radiosensitive tumors, such as Wilms' tumor, Ewing's tumor of bone and lymphoblastoma. Nemenow regards seminomas as more radiosensitive than lymphosarcomas. Oberndorfer likened the effects of radiotherapy on metastatic lesions from seminoma to that of snow melting in the sunshine.

Chevassu[20] mentioned the use of roentgen rays in his thesis on testicular tumors, but presented no details. Credit usually is given to Béclère[7] as the pioneer in this field. In 1905, he treated a patient who had an abdominal metastatic growth and who was cachectic when Béclère first saw him. The involved testis had been removed previously. The patient improved and lived fourteen months. The response was most remarkable as noted in Béclère's account. His reports on this case indicate that he used wave lengths of roentgen rays equivalent to about 50 or 55 kv., and that he applied 4 Holzknecht units to the skin of the abdomen weekly. The diagnosis, however, was not proved histopathologically. Later, Béclère[6] reported on the patients with metastasis whom he had treated between 1905 and 1911, and who had lived five years.

Pfahler reported 2 successful cases in which metastatic seminomas apparently were present, and in which treatment had been given prior to 1920. He used a potential equivalent to so-called moderate voltage.

After the extensive development of radiotherapy and the gradual increase in knowledge of various clinical aspects of testicular tumors, the pioneer efforts of Béclère and others seem a far cry from present treatment for seminoma of the testis. Barringer stated that the response to irradiation of some metastatic masses from testicular tumors is so spectacular and dramatic that one is forced to realize the importance of this revolutionary change in the treatment of testicular tumors. According to Barringer,[4] it has become obvious that the present methods of treatment for testicular tumors have caused surgical intervention to assume a secondary importance to irradiation, and its value in some cases is open to question.

As is the case with pathologic and other classifications of testicular tumors, a classification of the methods of radiotherapy for these tumors also is difficult. It has been said that there are as many pathologic classifications of testicular tumors as there are pathologists, and it might be stated with equal truth that there are as many radiologic techniques for treating testicular tumors as there are radiologists. This, of course, is an exaggeration and perhaps the variations in each case and the differences in minor details have led to this conclusion. Pathologic and irradiation data are so variable that it is difficult to compare results, and many otherwise satisfactory reports cannot be evaluated because they merely mention the use of roentgen therapy with-

out discussing the actual technique employed. In general, the technique of roentgen therapy varies with the type of apparatus available to the particular radiologist and with the fashion of roentgen therapy in vogue at the time of the report. The earlier results and methods naturally dealt with roentgen therapy carried out with relatively small doses and with rays of longer wave lengths and less penetration than those now in use. On the other hand, reports of techniques in which potentials approaching supervoltages were used are to be found in the modern literature.[58] Newell[77] and Desjardins[32] both recently called attention to the fact that the evaluation of roentgen therapy, by the laity and the majority of physicians, is almost entirely in terms of numbers signifying voltage, and the state of affairs is such that the magnitude of the voltage and the complexity and size of equipment seem more important than the clinicoradiologic approach to the patient.

A trend toward the protracted fractional method of roentgen therapy also is noted.[44,100] For the American views on roentgen therapy for seminoma of the testis and other testicular tumors, one is referred to the works of Dean,[27] Ferguson,[44] Hinman and Powell,[62] Desjardins and one of us (E.T.L.), MacKenzie and Ratner, and Waters; and for its status in Europe, those of Nemenow, Bloom, Chwalla, Blümel, and Porchovnik and Treister.

Preoperative Roentgen Therapy. Preoperative roentgen therapy is advocated particularly by Dean,[25] Ferguson,[44] and Randall and Bothe. Dean[27] presented statistics to demonstrate that, in his group of all types of testicular tumors, the survival rate for the patients who had received preoperative irradiation was higher than that for patients who had received irradiation only after orchidectomy. In Dean's technique, as will be shown, orchidectomy usually is performed five or six weeks after roentgen treatment has been begun and after total irradiation of the involved testis. Of the same school of thought, Ferguson admitted that probably there would have been no difference in the end-results among patients treated preoperatively and among those treated postoperatively if these patients had received treatment shortly after operation. Apparently, among some of the patients who had received treatment after operation, too long an interval had elapsed between the operation and treatment, because Ferguson mentioned that, on the part of both surgeon and patient after orchidectomy there is a tendency to procrastination about roentgen therapy. From the fact that it is not generally employed, we gather that a definite advantage from preoperative irradiation has not been demonstrated and that there are certain disadvantages and hazards to the procedure. The usual objections are that the accuracy of clinical and biologic diagnosis is subject to great error, and that because irradiation distorts the histologic pattern it is often difficult to make a histopathologic diagnosis when the tumor is finally removed. In opposing preoperative irradiation, Hinman[62] questioned if the cases in Dean's[27] series, in which the results apparently were better, were all cases of malignant testicular tumor.

From Dean's[27] description of the specimens removed after irradiation, it is evident that the contention that the diagnosis cannot be proved microscopically may be valid. At times, a necrotic mass was seen, in which the outlines of cells were visualized poorly; later, caseous masses formed and the lesion could not be diagnosed. Occasionally, a hematoma was found to replace the tumor, and occasionally a fibrous reticulum poor in cells was seen.

That time is lost during preoperative irradiation and that, during this period, malignant cells may be escaping from the primary tumor are claims made by those who oppose preoperative irradiation. They claim also that there is danger of sterilizing the remaining testis during irradiation of the involved side. Some efficient protective device, such as the protection clamp for the testis, devised by Desjardins,[30] could easily be used to overcome this danger and this

objection. The alleged danger of disturbing and disseminating malignant cells by orchidectomy without preceding radiotherapy appears far less serious during removal of a cancerous testis than during removal of a cancer elsewhere in the body, because the spermatic cord is rarely involved. If reasonable care is taken during orchidectomy, and the spermatic cord is sectioned initially, it is not likely, in view of the anatomic arrangement of the testis, that further dissemination of malignant cells would occur. Preoperative irradiation is opposed by a number of recent authors, including Smith, Dresser and Mintz, Grevillius, Hinman and Powell,[58,62] and MacKenzie and Ratner.

Radium Therapy. Historically, the use of roentgen rays preceded the use of radium in the treatment of testicular tumors. Early in the third decade of this century, however, several reports concerning the use of radium were made by Barringer and Dean, Bowing, and Dean.[26] The last named author described, in 1925, a technique for treating the retroperitoneal lymph nodes in cases of metastasis from testicular tumors, in which he used a 4 gm. radium pack, administering 8,000 mg-hr. at 6 cm. through a filter of 0.5 mm. of silver and 2.0 mm. of brass. Bowing used smaller doses. As the extent of the manifestations of these tumors throughout the body became better known, and as roentgen therapy was proved to be a suitable treatment for other kinds of tumors, it was gradually found that roentgen therapy was more practical, efficient and expedient than radium for treating these tumors. After reviewing a number of current works on both urology and radiotherapy, we have concluded that, at present, radium is not generally used in treatment of testicular tumors. Its use should perhaps be limited to the treatment of localized metastatic growths, such as those in the supraclavicular space, of Virchow's node, or of a small, recurrent tumor, rather than to the common extensive metastatic changes in the abdomen.

Present Technique of Roentgen Therapy. A representative plan of roentgen therapy for the more radiosensitive testicular tumors is embodied in the technique cited by Ferguson and Dean,[27] and is the plan which is probably in current use at Memorial Hospital in New York.

This method of irradiating testicular tumors comprises preoperative treatment, in which the primary testicular tumors receive three doses each of 300 r every three days, delivered at a potential of 200 kv., with 25 milliamperes of current, a 50 cm. target-skin distance, and with a filtration of 0.5 mm. of copper and 1.0 mm. of aluminum, until 1,500 to 1,800 r has been given. With similar factors, except that the distance is increased to 70 cm. the lower, middle and upper, or epigastric, regions of the abdomen are treated anteriorly and posteriorly, two of these six fields receiving 300 r daily until 2,000 or more roentgens have been given to each field. The abdomen is treated regardless of the presence or absence of demonstrable metastasis. If metastasis to the lungs or mediastinum has occurred, these regions also are treated; four anterior and four posterior fields are used and from 1,600 to 1,800 r is administered to each field. Orchidectomy is performed about five or six weeks after irradiation of the primary growth. There is a great deal of variation in each case, and the plan of treatment is altered to suit varying needs. Adequate follow-up examinations are made periodically; physical examination and roentgenograms of the thorax are made, particularly in the first year.

Smith, Dresser and Mintz advocated a generally similar course of treatment, but they advised primary orchidectomy and postoperative irradiation. Peirson,[83] Herger and Thibaudeau, Wesson, Waters, and others, use slight modifications of the general plan of treatment. In the main, the voltages reported to be used by American radiologists vary from 180 to 200 kv. The quality of radiation is essentially the same as Dean's[27] and the anterior fields generally include the abdomen. Doses vary from 200 to 400 r per field per treatment, with total doses to each field ranging from 800 to

3,000 r. In the absence of demonstrable metastasis the thorax is rarely treated. The method and number of after treatments varies somewhat according to the needs of each patient.

The present methods of roentgen treatment for testicular tumors in use in Europe have been reviewed by Chwalla. In Italy, Blefari-Melazzi used fractional methods over a period of twenty-five days. Porchovnik used smaller doses than are usually given. Blümel used a plan which does not differ much from that employed by Ferguson.[44] Grevillius, who published an excellent study of malignant testicular tumors, did not discuss the details of roentgen treatment but advised its use in every case of malignant testicular tumor.

In reviewing the common techniques of roentgen therapy for seminomas of the testis, potentials in the region of 180 to 200 kv. ("high voltage" or "deep therapy") are used almost universally today. There is an increasing number of installations of so-called supervoltage roentgen machines ranging in potential from 400 to 1,000 and more kilovolts. As the methods of treatment in vogue at such centers seem to demand the use of these "super potentials," some testicular tumors are being treated with techniques in which these voltages are used.[58] It is too early to know what effect these relatively new developments will have, but it is probably safe to say that increasing knowledge of the extreme radiosensitivity of seminomas should and will limit the use of supervoltage therapy, because, with ordinary methods, sufficient radiation apparently reaches the tumor cells of both the primary and metastatic lesions to produce satisfactory reactions in them. We shall not discuss further the relative value of supervoltage therapy, but will quote a statement by Failla[39] published in 1938 in regard to this type of treatment:

> Our experimental findings indicate that supervoltage X-rays have the advantage of being biologically less effective on the skin, to an extent approaching that of gamma rays. They possess an advantage over radium packs in that the high intensity available permits the use of longer source-to-skin distances than are possible with the amounts of radium at our disposal. However, this introduces an element of danger in that the use of target-skin distances commonly employed with 200 kv. X-rays, and particularly longer ones, may result in too severe damage to internal structures. The adjustment of the physical factors in the treatment of a given patient with supervoltage X-rays requires much greater care than in treatment with 200 kv. X-rays, and in either case much more information than we now possess.

Since the advent of the technique of protracted fractional doses of roentgen rays, this method, or some modification of it, has been widely used. In a large number of institutions, it has replaced entirely the single massive dose method in the treatment of various types of malignant neoplasms. The efficacy of this method in the treatment of epidermoid carcinoma in certain regions of the body, particularly in the pharynx or larynx, generally is admitted, but there are certain reasonable arguments against its use in the treatment of seminomas of the testis and their metastatic deposits. The risks of transferring the technique of prolonged, intense, fractional irradiation for a hard epidermoid carcinoma of the pharynx, for example, to the treatment of epigastric metastatic deposits from a seminoma of the testis, are not hard to imagine, if the reactions of the irradiated mucous membrane in the treatment of a carcinoma of the pharynx are familiar. Perhaps even more severe reactions might be produced in the sensitive mucosa of the gastrointestinal tract. We have previously compared the great radiosensitivity of seminomas of the testes to that of lymphoblastomas. Roentgen therapy of lymphoblastomas is not carried out by the protracted fractional method in many large centers, as far as we are able to determine from a study of contemporary radiologic literature. This state of affairs also may be a valid argument, by analogy, against this type of treatment for seminomas of the testis.

The fact that seminoma of the testis is one of the most, if not the most, radiosensitive tumor, is universally accepted. In 1925, Nemenow said he suspected that intense irradiation of the metastatic seminomas from the testis produced more radioresistant residual metastatic masses than did milder treatment. He did not prove this, but merely stated his impression.

Desjardins, Squire and Morton, and Desjardins and one of us (E.T.L.) discussed the treatment of testicular tumors by a method which differs in essentials from the types in general use. This plan has been used in the treatment of the cases which form the basis of this study.

Treatment of Seminomas at the Mayo Clinic. Because of the nature of the conditions under which they were treated, our patients have been handled by the same group of medical consultants and surgeons, and treatment was administered by the same group of radiologists. In general, the ordinary treatment of testicular tumors at the Mayo Clinic is primary orchidectomy followed by roentgen treatment. This scheme, of course, is modified to meet the needs in each case. On all of the patients included in our series (those with or without metastatic processes and with or without fully descended testes), operative removal of the involved testis was performed. It is the general policy of the surgeons at the Clinic to advise removal of an involved testis, except perhaps in late cases, even in the presence of metastatic involvement. This is done because, even in cases in which metastasis has occurred, excision of the involved testis eliminates the late local complications of a large, heavy, sloughing and infected scrotal tumor, in addition to giving a histopathologic diagnosis, and perhaps also a better prognosis.[88] A theoretical possibility justifying this procedure is that removal of the primary tumor may be followed by regression of the metastatic processes. A minor consideration, which is less theoretic but still is not proved, is that removal of the tumor eliminates a focus from which further tumor cells might disseminate.

After a relatively short postoperative convalescence, the patients are advised to undergo a series of roentgen treatments.

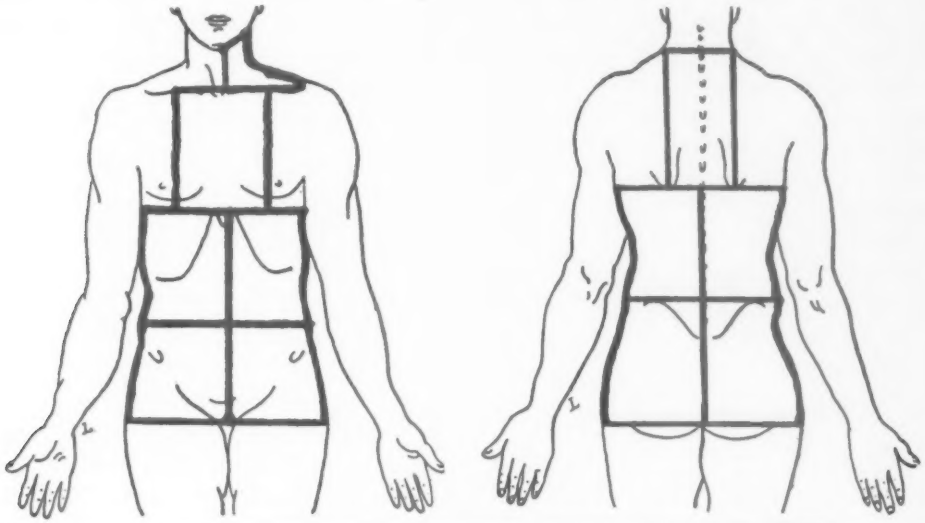
For a long time it has been the opinion of the therapeutic radiologists who have treated the patients in our series that all irradiation of seminomas of the testis and their metastatic processes is best carried out at potentials of the so-called moderate voltages (130–140 kv.). This opinion has been validated by a rather large experience. This selection of treatment is made because of the fact that there seems to be no definite proof of the superiority of higher voltages (particularly roentgen rays of 200 kv.) in the treatment of the lesions, because the extent of the paths of lymphatic drainage through which metastasis takes place often makes extensive treatment necessary, and because treatment with higher voltage results in intensive, unsafe and perhaps unnecessary irradiation of abdominal structures. Treatment in our cases, therefore, has been carried out with roentgen rays generated at potentials of 130 or 140 kv. and usually filtered through 6 mm. of aluminum (half-value layer equivalent to 0.32 mm. of copper). Usually four anterior abdominal fields extending from the xiphoid to the pubis and four corresponding posterior fields are used. The mediastinum and left supraclavicular space are irradiated routinely. Each field receives a dose of 540 r (measured in air) at skin surface. One or two fields are treated daily, depending, of course, on the patient's tolerance, and especially on the state of the formed elements of the blood. The course of treatment is repeated in one month, even though the patient is well clinically; occasionally, the course is repeated in two months (Fig. 6).

It has been found that the most common complication of irradiation of the trunk, and especially of the epigastrium, is leukopenia. It is generally regarded as axiomatic that the more intense the irradiation of the abdomen, the more severe are the

general reactions and the damage to the formed elements in the blood. Comparing the results of this technique with those obtained by others, we feel that the use of higher voltages or more intense treatment generally is not indicated in the treatment of seminomas, since not only do the results of the former technique seem better, but since it entails less risk to the patient.

The doses used at the Mayo Clinic in the treatment of seminomas of the testis are relatively low in comparison to those used elsewhere. Nevertheless, the statement that they are effective is confirmed by the statistical studies of Cabot and Berkson on the results in the treatment of these lesions.

Comment. Since, as demonstrated by many authors, seminoma of the testis responds to irradiation, an obvious corollary can be drawn, namely, that the therapeutic test can often be used to judge the nature of metastatic lesions from a testicular tumor of unknown histopathologic structure. We have not met this circumstance in the present series of 103 cases of seminoma of the testis, since in all cases the diagnosis was confirmed histologically. It is well known, however (and has been emphasized by Desjardins[34]), that the therapeutic test can be used with high accuracy in the differential diagnosis of seminomas of the testis.



TREATMENT FACTORS

FIELDS	KV	FILTRATION (mm) TOTAL	DISTANCE	MA	TIME	r/m Air	HVL mm
ALL	130	6.0 Al	40 cm	6	20	27	.32 Cu

Fig. 6. Scheme of postoperative roentgen therapy of seminomas of the testis.

It has been pointed out repeatedly, both in this study and elsewhere, that in any review of the literature on testicular tumors, especially in a review in which the histopathologic diagnosis and terminology are subject to as much variation as in cases of seminoma, great difficulty is encountered in evaluating any method of treatment. To us it seems apparent that, after reviewing urologic, surgical or radiologic literature on testicular tumors, the variations in the percentile distribution of the various histopathologic types of testicular tumors which are reported cannot be real. The discrepancies in the data given in various series of cases may be traced, in part at least, to the fact that the histopathologic diagnosis

of the tumor has been passed on by a number of pathologists, each using a different terminology. However, in trying to evaluate roentgen therapy or even the degree of response of these tumors to irradiation, it is our belief that, after due consideration of other published data, there probably is less variation in our particular group of cases of seminomas of the testis because of the fact that all 103 pathologic diagnoses were made by Broders and that all treatment was carried out by the same therapeutic radiologists, who used a fairly constant technique.

We offer this study for consideration of the data from the only series of cases of seminoma of the testis that have, in our opinion, uniformity of histopathologic diagnosis and uniformity of treatment and in which the end-result is known.

RESULTS OF ROENTGEN TREATMENT OF SEMINOMAS OF THE TESTIS

The results of treatment and the survival rates in two groups of cases of testicular tumors have been published by Cabot and Berkson, and by Desjardins and one of us (E.T.L.). We shall quote figures from these studies only as they pertain to the radiosensitivity of the tumors considered. We have selected five year survival rates from the work of Cabot and Berkson, since that criterion is widely used in evaluting the treatment of testicular tumors. In all cases of seminoma of the testis the survival rate was 67.7 per cent for five years, as compared with that in cases of all other malignant tumors of the testis, in which the corresponding rate was 29.3 per cent. Of all patients who had seminomas and who received roentgen therapy, 71.1 per cent lived five or more years. Of those patients who did not receive roentgen therapy, the survival rate was 58.8 per cent for the same length of time. Other types of testicular tumors, on the contrary, did not reveal such a good result. That irradiation has a favorable effect on the survival rates in those cases in which clinical evidence of metastasis was found at the time of the initial examination is attested to by the fact that 42.9 per cent of all patients who had seminomas with metastasis lived five years or more, as compared with 14.5 per cent of the patients who had other tumors (Cabot and Berkson's study), and as compared with the previously quoted statistics of Tanner and Wasterlain, whose five year survival rate was approximately 6 per cent for testicular tumors of all types.

Statistically, according to Berkson, there is a definite dividing line between seminomas and other types of tumors of the testis after roentgen therapy. We should like to note here that statistical studies, when presented only in brief as we have presented them, are subject to criticism when not fully qualified with the description of the subdivision.

However, it is neither the purpose of this presentation to make a statistical analysis of survivals nor to establish rates of cures but only to emphasize the difference in the radiosensitivity of seminomas in contrast to that of other malignant testicular tumors. By their response to irradiation, seminomas of the testis are a definite entity. As a result of this difference, they are paradoxically, in spite of their high grade of malignancy, the most favorable type of testicular tumor. Seminomas may be advanced, therefore, as an example of the parallelism between high malignancy with its concurrent undifferentiation and high radiosensitivity.

SUMMARY AND CONCLUSIONS

A primary purpose of this study was to determine what characteristics distinguish seminomas from other tumors of the testis. It is apparent, from the analysis of various objective points in the history and clinical examination of 103 proved cases of seminoma of the testis which we have presented, that there are no detectable data in the family history, the side of involvement, the anatomic location of the testis or the presence or absence of other local pathologic

processes, such as hydrocele or varicocele, that aid in the clinical diagnosis of seminoma of the testis. Also, the size, shape and consistence seem to have no definite or constant characteristics. The age of any given patient contributes little to the likelihood of correct diagnosis. In large groups of cases, however, the peak of maximal incidence of seminomas of the testis tends to fall at a later age than that of teratomas. There seems to be no rule that can be established in regard to metastasis, other than that the commonest site of metastatic lesions is the abdomino-aortic group of lymph nodes and that metastasis occurs early in the course of the disease.

From our analysis, we found that the only certain diagnostic procedure for the establishment of the presence or absence of seminoma of the testis is the demonstration of the characteristic histopathologic structure of the tumor by microscopic examination of excised tissue, for this seems to be the only characteristic by which it may be positively identified.

Seminoma of the testis is the commonest type of testicular neoplasm and, histopathologically, it is a definite entity. It is our opinion that the seminoma is a highly undifferentiated adenocarcinoma, and from the recently published investigations of several workers on the pathogenesis of the tumor, it no longer can be considered as belonging to a related group of tumors of the seminal epithelium but must be thought of as an independent type of neoplasm occurring in the testis.

For the present, analysis of the urine for gonadotropic substances does not offer definite aid in the diagnosis or management of a given case of seminoma of the testis, at least not when the tests are performed under the conditions and facilities generally available. Hormonal analyses are at best unreliable as far as the diagnosis of seminoma of the testis is concerned, although it is true that there is evidence to show that, in some instances, seminoma of the testis varies from other testicular tumors in the results obtained from hormonal analyses of the urine. These facts again substantiate the statement that this tumor is a separate entity.

Statistically, from the excellent response to roentgen therapy in our 103 proved cases and many others in the literature, seminomas of the testis differ from testicular tumors of other types in a definite manner. This fact has brought the test by roentgen treatment to a position secondary only to the histopathologic examination of the tumor for establishing a diagnosis of seminoma of the testis.

Roentgen therapy has assumed a position of primary importance in the management of these tumors and has altered the prognosis in cases of seminoma of the testis from one of hopelessness to one of subdued optimism.

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THE RESULTS OF ROENTGEN THERAPY FOR METASTATIC NEOPLASMS*

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THIS study of 432 cases with distant metastasis from malignant tumors was undertaken to compare the fate of the patients who had been given roentgen treatment for their metastasis with the fate of the patients who had not received any such treatment. Desjardins, Craver, Leddy, Schinz, and other authors, have repeatedly emphasized the great value of roentgen treatment in bringing palliation to patients suffering from cancers which do not permit any hope of a lasting cure. In this paper comprehensive statistical data will show to what extent the unfortunate patient with distant metastasis may hope to benefit from irradiation.

MATERIAL

All cases with distant metastasis observed at the Radiotherapeutic Institute of the University of Zurich during the ten year period from 1930 to 1940 are considered in this study. There are 201 males and 231 females; their average age is 55.3 years. The youngest patient is one year of age and the oldest seventy-nine years of age.

The site of the primary growth is given in Table II. There is only a small number of cases with tumors of the digestive tract, the skin and the female genital organs because these patients are for the most treated in other departments. The treatment of the primary growth by operation or by irradiation or by a combined method resulted for only one-half of the patients in a regaining of their full health for a certain time. Thirty-six cases were in too poor general condition to be submitted to any specific treatment.

Histopathology. The group of squamous cell and epidermoid carcinomas was largest, with 180 cases of this type; there were also 13 adenocarcinomas, 10 melanomas, 7 seminomas, 14 malignant strumas of the Langhans type, and 36 carcinomas not specifically listed. There were only 36 sarcomas because all malignant lesions of the lymphoblastoma type are strictly omitted from this study. The influence of the histopathology upon the reaction to treatment was evident from the exceptionally favorable results obtained in some of the seminomas and the extremely poor results from treatment of melanomas. For other histopathologic types of primary growths the dependence of the reaction on treatment of the metastasis was less clear.

The site of the metastasis is given in Table I. One-half of the cases with metastasis to the lungs and a little more than one-half of the cases with metastasis to the bones did not have any other metastasis. The rest of the cases had metastasis in several of the systems listed; these cases are registered in each group separately. All cases with metastasis to the liver are included in the group of "the other organs," since the response to treatment was essentially the same for all these cases.

The interval between the discovery of the primary growth and the metastasis averaged 11.2 months. More than one-fourth of all patients, however, already had metastasis when first seen by the doctor. And in another half of all cases the metastasis developed within the first year after the diagnosis of the primary growth. On the other hand, there are 41 patients with an interval of more than three years; the longest interval was ten years. In all cases with an interval of more than five years the metastasis was from cancer of the breast.

IRRADIATION

The number of cases treated is given in Table I. The rules for selecting our cases

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for treatment are given in detail at the end of this paper.

The method we usually used was the fractional one. The factors were as follows: 180 kv., 6 ma., filter 0.75 mm. copper, target skin distance 50 cm., dosage 240 r, measured in air, daily for ten to thirteen doses. In a very few instances the protracted fractional method and in a few more instances irradiation of the entire thorax was used. The general results of these two methods, however, did not warrant their wider use. Metastasis to the skin was frequently treated with a single massive dose of 1,250 r, measured in air.

TABLE I

SITE OF METASTASIS, FREQUENCY OF TREATMENT PERCENTAGE OF FAVORABLE LOCAL REACTION

Site of Metastasis	Total Cases No.	Treatment Given		Favorable Local Results Per Cent
		No.	Per Cent	
Lungs	181	51	28	61
Bones	208	145	72	78
Skin	80	54	67	77
Others	81	22	28	14

RESULTS

Since complete cure is impossible we shall try to judge the palliative effect of radiotherapy on distant metastasis by the following three criteria: (1) the influence on the local metastatic growth; (2) the influence on the survival time; (3) the influence on the duration of the patients' well-being. This last point must be considered the most important one.

Local Results

The diminution is size of the metastasis or the complete alleviation of local pain must be considered a favorable local result because it has not been the aim of the treatment to make the metastasis disappear completely. Table 1 gives the frequency of this occurrence and the frequency of treatment for the four main sites of metastasis A treated case is one that has received treatment for the type of metastasis under consideration; it may or may not have received treatment for other types of metastasis. The percentage of favorable local results refers to the total number of single metastases treated in each group.

The best local results are obtained from treatment of metastasis to the bones and to the skin. The treatment of metastasis to the lungs was carried out in only a small percentage of such cases but gave good local results. The cases treated in this group were mainly those with hilar metastasis, with solitary lung metastasis and with metastatic pleurisy. The high radiosensitivity of metastasis from seminomas is confirmed by our results. The treatment of metastasis in all other organs except the bones, the skin, or the lungs, gave satisfactory results in only a small percentage of the metastasis treated.

Duration of Life. The survival time of treated and untreated cases together is given in Table II; the death rate after one, three, and six months is appallingly high, regardless of the site of the primary growth. On the other hand, several cases lived for more than two years. It must, however, be noted that in all these patients the metastases were from primary growths in a glandular organ: the breast, the testicle, the prostate, or the struma.

The average length of life of the patients is related to the interval between the discovery of the primary growth and the first metastasis only insofar as the average length of life of the cases with an interval of more than two years has reached 15.1 months and thus is almost twice as long as the average of 8.1 months for all cases with an interval of less than two years. The average length of life of each group with an interval of zero, three, six or twelve months, does not, however, differ for more than one month from the total average of all these cases together.

It is interesting to compare the survival period of the treated cases with that of the

TABLE II

SITE OF PRIMARY GROWTH, DURATION OF LIFE SINCE DISCOVERY OF FIRST METASTASIS

Site of Primary Growth	Cases No.	Patients with a Survival Time of											
		1 mo.	3 mo.	6 mo.	1 yr.	2 yr.	3 yr.	4 yr.	5 yr.	6 yr.	7 yr.	8 yr.	9 yr.
Skin and supporting tissue	12	3	5	3	1	—	—	—	—	—	—	—	—
Melanoma	10	3	4	1	2	—	—	—	—	—	—	—	—
Mouth and pharynx	66	25	17	19	5	—	—	—	—	—	—	—	—
Lungs	8	6	1	1	—	—	—	—	—	—	—	—	—
Struma	48	19	5	9	9	3	2	—	—	1	—	—	—
Breast	178	34	36	55	37	10	2	3	1	—	—	—	—
Intestinal tract	40	25	9	6	—	—	—	—	—	—	—	—	—
Kidneys	7	2	1	2	1	1	—	—	—	—	—	—	—
Prostate	26	9	7	5	4	—	—	—	—	—	1	—	—
Testicle	14	6	3	2	—	1	1	—	—	—	—	1	—
Female genital organs	10	4	4	1	—	1	—	—	—	—	—	—	—
Unknown primary growth	13	3	4	3	—	3	—	—	—	—	—	—	—
Total		139	96	107	59	19	5	3	1	1	1	1	0

untreated ones. We must, of course be very cautious in crediting the treatment for the in every respect considerably better figures for survival of the treated group (Table III–VII), since this is likely to be, at least partly, due to our method of selecting the cases for treatment. Two facts concerning the survival period do, however, deserve special attention: (1) only treated cases have lived for more than three years, and (2) the difference of the survival rates and of the average duration of life in favor of the treated cases is larger in those groups of metastasis that had also given the higher percentage of favorable local results. These two facts prove that the treatment may influence the survival period favorably and that it may give hope for a duration of life of more than three years, at least in some cases with metastasis from tumors in glandular organs.

Duration of Well-being. The most important criterion for the value of irradiation of metastases is the frequency with which the patient's well-being can be restored or prolonged. The patient's condition is, of course, dependent on many other factors beside the metastasis. We believe in considering the patient as an individual with but one health and therefore we feel justified in calling the treatment successful only if the patient's well-being after treatment of the metastasis is neither disturbed by the metastasis nor by any other reason. On the basis of this belief we shall consider as *well* only a patient who can continue his normal activity without any substantial complaints.

Our data are based on the case histories and the very thorough follow-up records of all cases. The decision as to whether a patient should be called well was made as objectively as possible and always by the same observer; the histories were, of course, taken by several men. By limiting our judgment to the two possibilities of well or not well for the patient, we had necessarily to drop from the group of favorably influenced cases all those who were slightly improved but had not regained their full well-being. The time of treatment has always been counted as a period of not being well.

Several patients had had multiple metastases some of which had been given roentgen treatment, and others had remained untreated. These cases are listed in both the treated and the untreated group and their duration of life and of well-being is registered separately from the time of de-

Table III

AVERAGE DURATION OF LIFE AND OF WELL-BEING FOR TREATED AND UNTREATED CASES

Site of Metastasis	Average Duration of Life (mo.)		Average Well-being (mo.)	
	Treated group	Untreated group	Treated group	Untreated group
Lungs	12.5	5.4	6.6	1.0
Bones	13.0	5.8	5.9	1.0
Skin	15.8	4.6	4.5	0.4
Other sites	4.7	3.6	0.7	0.4

velopment of the treated and of the untreated metastases.

The last columns in Tables IV–VII give the percentage of patients well among the living patients, that is to say the number of patients well at each of the times of investigation is related only to the number of patients then still alive. The mere rise in the percentage may be due to an excessive rate of deaths among the patients not well; the important point of these figures is the *change in the difference* between the percentage of patients well in the treated group and that of the untreated group. The change of this difference proves conclusively the positive or negative influence of the treatment upon the frequency of well-being among those patients.

Metastasis to the Lungs. The average time of well-being for the treated cases exceeds that of the untreated cases to a considerable extent (Table III). The number of patients well in the treated group increases immediately after treatment; from then on the number of the patients well decreases faster in the treated group during the first six months and faster in the untreated group during the later periods (Table IV). The percentage of patients well among the patients living is substantially higher for the treated group. This fact is all the more important since before treatment the relation of the percentages was just the opposite. A very high percentage of the patients living for more than two years have been well for a very long period of their lives; all these cases have had treatment and have not been well before treatment. These results give evidence of the favorable influence of the treatment; in evaluating the merits of treatment it must, however, be borne in mind that a comparatively small number of all cases with metastasis to the lungs have been selected for treatment. The cases giving the best results as to the restoration of the patient's well-being are mainly those with metastases from seminomas, from malignant struma of the Langhans type, and cases with metastatic pleurisy.

Metastasis to the Bones. The average

Table IV

METASTASIS TO THE LUNGS: PATIENTS WELL AND PATIENTS LIVING: PERCENTAGE WELL VS. LIVING

Time	Number of Patients				Percentage of Patients Well Among the Living	
	Well		Living			
	Treatment	No treatment	Treatment	No treatment	Treatment	No treatment
Before treatment	4	19	51	130	8	15
After 1 mo.	21	19	51	130	41	15
After 3 mo.	17	15	42	76	40	19
After 6 mo.	12	13	34	43	35	30
After 1 yr.	8	3	18	13	45	23
After 2 yr.	3	0	4	1	75	0
After 3 yr.	2	0	3	0	66	—
After 4 yr.	1	0	2	0	50	—
After 5 yr.	1	0	1	0	100	—

TABLE V

METASTASIS TO THE BONES: PATIENTS WELL AND PATIENTS LIVING: PERCENTAGE WELL VS. LIVING

Time	Number of Patients				Percentage of Patients Well Among the Living	
	Well		Living			
	Treatment	No treatment	Treatment	No treatment	Treatment	No treatment
Before treatment	19	7	172	69	11	11
After 1 mo.	77	7	172	69	44	11
After 3 mo.	56	6	128	45	44	13
After 6 mo.	33	4	92	31	36	13
After 1 yr.	23	0	50	13	46	0
After 2 yr.	6	0	23	3	26	—
After 3 yr.	3	0	8	0	36	—
After 4 yr.	2	0	2	0	100	—
After 5 yr.	1	0	2	0	50	—

duration of well-being was considerably longer for the treated cases (Table III). The number of patients well is greatly increased in the treated group immediately following treatment and the following decrease of the number of patients well is much slower in the treated group (Table V). The percentage of patients well was the same in both the treated and the untreated group before treatment was given; treatment produced a much higher percentage of patients well in the treated group than in the untreated one. This fact proves the favorable influence of the treatment. A very large number of cases with bone metastasis from all types of primary tumors responded favorably to roentgen treatment.

Metastasis to the Skin. The average duration of well-being is considerably higher for the treated cases (Table III). The increase in the number of patients well in the treated group immediately after treatment is not very remarkable; however, there are very few patients well in the untreated group (Table VI). The percentage of patients well in the treated group is considerably higher than in the untreated group already before treatment was given; after treatment this difference first increases a little but drops steadily thereafter. The fact that the well-being could be restored in only a

TABLE VI

METASTASIS TO THE SKIN: PATIENTS WELL AND PATIENTS LIVING: PERCENTAGE WELL VS. LIVING

Time	Number of Patients				Percentage of Patients Well Among the Living	
	Well		Living			
	Treatment	No treatment	Treatment	No treatment	Treatment	No treatment
Before treatment	20	4	54	26	35	15
After 1 mo.	28	4	54	26	52	15
After 3 mo.	19	1	45	15	45	6
After 6 mo.	11	1	31	7	38	14
After 1 yr.	6	0	19	3	30	0
After 2 yr.	2	0	8	0	25	—
After 3 yr.	1	0	5	0	20	—
After 4 yr.	1	0	4	0	25	—
After 5 yr.	1	0	1	0	100	—

few instances is not surprising since most of the patients in this group were not disabled by the skin metastasis but from other causes.

Metastasis to Other Organs. The average duration of well-being for both the treated and the untreated patients is less than one month (Table III). The number of patients well in the treated group increases immediately after treatment but after six months there are no more patients well in this group (Table VII). The percentage of patients well among the patients living increases in the treated group over the untreated group immediately after treatment but this relation is very soon reversed. The results in this group of metastases are not satisfactory: although only a small number of cases has been treated the well-being could be restored only exceptionally and never lasted for more than six months.

TABLE VII

METASTASIS TO OTHER ORGANS: PATIENTS WELL AND PATIENTS LIVING: PERCENTAGE WELL VS. LIVING

Time	Number of Patients				Percentage of Patients Well Among the Living	
	Well		Living			
	Treatment	No treatment	Treatment	No treatment	Treatment	No treatment
Before treatment	1	4	22	59	5	7
After 1 mo.	5	4	22	59	23	7
After 3 mo.	3	3	12	28	25	10
After 6 mo.	0	1	8	10	0	10
After 1 yr.	0	1	1	3	—	33
After 2 yr.	0	0	0	0	—	0

CONCLUSIONS

Roentgen treatment may favorably influence the well-being of the patient with distant metastasis and his survival time as well as the local metastatic growth. Because of the considerable difference in response to treatment the following three groups of cases must be separated:

(1) *Cases that must be given roentgen treatment.* This group includes the cases with metastasis to the bones from tumors of glandular organs, the metastasis to the lungs from seminoma and the hilar metastasis from malignant struma of the Langhans type. The general condition of the patient must, of course, not be altogether hopeless.

(2) *Cases likely to benefit considerably from roentgen treatment.* Belonging to this group must be considered all cases with bone metastases except those mentioned under (3), solitary metastasis to the lungs, carcinomatous pleurisies and metastasis to the skin. Generally speaking, this group comprises all cases where the metastasis gives rise to local discomfort.

(3) *Cases not likely to improve much after roentgen treatment.* In this group belong all cases with multiple metastases to the lungs except those mentioned under (1), all cases with bone metastasis from tumors of the pharyngeal region and of the lungs or from melanomas and all cases with metastasis in other organs except the lungs, the bones or the skin.

SUMMARY

Statistical data on 432 cases with distant metastasis from malignant tumors are given and the fate of the cases treated with roentgen irradiation is compared with the fate of the cases remaining untreated.

Local palliation can be brought about in 70 per cent of the cases treated; this corresponds to 45 per cent of the total number of cases.

The duration of life is generally longer for the treated cases. Only among the

treated cases do survival periods of more than three years occur.

The most important criterion for the usefulness of the treatment is the possibility of restoring and prolonging the patients' well-being. This aim has been reached in about one-half of all cases treated.

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ROENTGEN RAYS IN THE TREATMENT OF MALIGNANT TUMORS OF THE KIDNEY IN ADULTS*

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THIS paper deals with the results of roentgen treatment in 37 adult patients who were seen at the University Hospital with malignant tumors of the kidney. The first patient was treated November, 1927, and the last in March, 1937. All patients were traced and those now living have been observed from 60 to 120 months. The apparent improvement in prognosis of the preoperatively irradiated group of patients when compared with the postoperatively irradiated group and those receiving only irradiation warrants the reporting of these results even though the total number of patients treated is small.

The incidence of renal neoplasm in the adult is low, and the early diagnosis of such a lesion is exceptional. Reports in the literature indicate that these tumors consist chiefly of hypernephromas and adenocarcinomas in the approximate ratio of 9:1. In our series, nephrectomy done in 24 of the 37 patients revealed 21 hypernephromas and 3 adenocarcinomas.

The reported results of the surgical treatment of renal tumors in adults have been varied. Priestley[5] reported the five to ten year control of 35 per cent of those patients operated upon for epithelioma of the kidney. Thirty-eight per cent of those who had adenocarcinomas removed were controlled for a similar period. Some of these had an unstated amount of roentgen therapy. Others[1,4] have reported a five year survival rate of 5 to 15 per cent of patients treated only by nephrectomy.

Waters[6] has reported that the five year survival rate has increased from 5 to 15 per cent to approximately 32 per cent for those patients who had preoperative roentgen treatment. In our experience also roentgen therapy has been of therapeutic assistance. Patients receiving what is considered adequate preoperative irradiation apparently have a better outlook than those with only postoperative therapy. Eight out of 10 patients in the preoperative group have been controlled five or more years against 3 out of 14 in the postoperative group. We think, therefore, that these findings indicate the value of adequate preoperative roentgen irradiation. Furthermore, the urologists of this institution tell us that nephrectomy is made easier because irradiation has reduced the vascularity of the renal neoplasm. Waters has observed considerable regression in the size of the irradiated neoplastic kidney. In our series, however, roentgen therapy had very little effect upon the size of the tumor mass.

TABLE I

	Living and well 60 mo. or more	Dead	Living with disease
Group I (preoperative roentgen therapy followed by nephrectomy)	8	1	1
Group II (postoperative roentgen therapy)	3	11	0
Group III (roentgen therapy only)	1*	11	1
Total	12	23	2

* See discussion for details.

As indicated in Table I there were 10 patients in Group I who received what was considered an adequate amount of preoperative roentgen therapy. Of these, 1 patient died of his disease thirty-three months after irradiation. Eight who are living and apparently free of disease have been observed from sixty to eighty-two months. The remaining case in this group has lived eighty-three months, but pul-

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monary metastases have been present for the past eighteen months. The pathologic diagnosis was hypernephroma in 9 of these, while an embryonal adenocarcinoma of the kidney was diagnosed in the patient who is living with evidence of metastases.

The factors and technique used in the preoperative group were as follows: 200 kv., 20 ma., 50 cm. target skin distance, Thoraeus filter (equivalent to 2 mm. Cu). The size of the field was determined by the size of the mass and was either 10 × 15 cm. or 15 × 15 cm. The kidney was irradiated through anterior, lateral and posterior fields. Care was taken to place the lateral field far enough posteriorly to cover the kidney mass. A daily dose of 200 roentgens (measured in air) was given to each of two fields for six days per week and the total dose through three fields averaged approximately 5,600 r (measured in air). The smallest dose administered was 4,000 r (in air) while the largest was 9,000 r. Only 1 patient had two series of treatments and these were given within a period of eight weeks. All the rest had one course.

Nephrectomy was done approximately fourteen weeks after completion of roentgen therapy. One patient underwent operation eight weeks after treatment and the longest interval between irradiation and surgery was fifty-six months. This woman refused operation after irradiation, but went elsewhere fifty-six months later for removal of what proved to be a hypernephroma. At last report, eighty-two months after roentgen therapy, she is living and well. We think, however, that an interval of eight to ten weeks between irradiation and surgery is adequate.

There were 14 patients in Group II who received roentgen therapy after nephrectomy. Irradiation was usually begun about three weeks following removal of the kidney. Of the 14 patients 3 are living and well sixty-one, seventy-one, and eighty-four months after completion of therapy. The remaining 11 are dead with periods of survival ranging from a few weeks to seventy-eight months. Seven of the 11 of this group who are dead, lived from a few weeks to forty-four months after receiving treatment. Death in each case was believed to be due to metastases. The histopathologic diagnosis in this group included 10 hypernephromas and 2 papillary carcinomas of the kidney pelvis. No microscopic diagnosis was made in 2 cases. In each of these, however, the gross diagnosis was hypernephroma and the patient apparently died of malignant disease. Two of the 3 survivors had proved hypernephromas, while the third had a papillary carcinoma of the renal pelvis.

Postoperative roentgen irradiation technique was as follows: 11 of the 14 cases were treated with 180 or 200 kv., 5, 8, or 20 ma., depending upon the apparatus used, 50 cm. distance, Thoraeus filter, with varying sized anterior and posterior fields. These were 10 × 15 cm., 15 × 15 cm., and 20 × 20 cm. A dose of 200 r (in air) was given daily to each field for six days a week with an approximate dose totalling 4,200 r. There were two exceptions to this statement, inasmuch as 2 patients received 800 and 1,200 r (in air) respectively. Although these doses are considered inadequate, 1 patient lived for a few weeks while the other survived twenty-seven months before dying from metastases. The majority of the 14 cases had but one series of treatments, although a few did have divided series of 1,200–1,500 r repeated three times over a period of twelve months. In one instance, a patient was given a total dose of 8,000 r (in air) in multiple courses over an interval of twelve months.

Three patients in this group were treated with 140 kv., 5 ma., 40 cm. distance, a filter of 0.25 mm. Cu and 1 mm. Al, through anterior and posterior fields which varied in size from 8 × 10 cm. to 18 × 20 cm. The total dose in air through the two fields was 4,000 r.

Group III consists of 13 patients in whom the only treatment was roentgen irradiation. In 11 out of the 13 patients an effort was made to eradicate the lesion, even though it was considered inoperable. Of

these 13, one patient has lived 120 months and remains apparently free of neoplasm while another has survived eighty-two months but now has evidence of active tumor. The remaining 11 are dead and most of these died within thirty-six months after completion of therapy. However, 2 patients lived sixty-six and eighty-eight months respectively. The follow-up in all cases revealed that death was due to neoplasm. The diagnosis of hypernephroma or other malignant kidney tumors in any case in this group is open to doubt since microscopic examination was not done. Two of these patients underwent exploration with the gross findings of a malignant renal tumor but no tissue was obtained for microscopic examination. The diagnosis in the other cases was determined from the history, physical examination and pyelograms.

The technical factors of treatment in this group were: 180 or 200 kv., 5, 8, or 20 ma., 50 cm. distance, 0.5 mm. Cu or Thoraeus filter (2.0 mm. Cu equivalent), anterior and posterior fields which varied in size depending upon the size of the mass. These included 10 × 15 cm., 15 × 15 cm., and 20 × 20 cm. areas. A daily dose of 200 r (in air) was given to each anterior and posterior field for six days a week until a total dose of 4,000 r through the two areas was obtained. Six out of the 11 received this dosage in one series while one had 5,000 r, and another 7,200 r in one series. Two patients received a total of 8,000 r in two series over a period of ten months. Two patients received what we believe to be inadequate dosage, namely 1,400 r and 2,200 r through anterior and posterior fields. One of these patients lived but one month while the other survived sixty-six months. Since Carlson and Ockerblad[3] report an untreated hypernephroma of ten years' duration, and we have seen cases of hypernephroma that have survived ten to fourteen years without treatment, we place no great significance on this unusually long survival period.

SUMMARY AND CONCLUSIONS

A series of 37 adults who were treated for neoplasm of the kidney is reported. These are divided into 3 groups: (I) those having roentgen therapy prior to surgery; (II) those irradiated after nephrectomy, and (III) those receiving only roentgen therapy. Twelve of the 37, or 31.6 per cent, are living sixty or more months without evidence of residual or metastatic disease. One patient has been followed for 120 months. Eight of the 12 survivors, or 66.7 per cent, had preoperative roentgen irradiation. While this number is obviously too small to warrant any dogmatic statements, it is thought that these results indicate the value of the preoperative use of roentgen rays. It appears that in those operable cases, preoperative roentgen therapy improves the prognosis while postoperative roentgen therapy apparently has nothing more to offer than surgical removal without irradiation. Roentgen irradiation also makes nephrectomy easier by decreasing the bleeding at operation. Roentgen therapy without surgery is not believed to be curative and is not recommended even though one patient so treated has survived 120 months.

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OBSTRUCTIVE PHENOMENA ASSOCIATED WITH PRIMARY BRONCHIAL CANCER

REPORT OF UNUSUAL CASE

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ROENTGENOSCOPY is of great value in detecting growths arising in the bronchi. At times, a malignant tumor may be fairly well defined by roentgenoscopy, but more often the opaque shadow in the roentgenogram is much larger than the mass constituting the tumor. In the case of benign tumor or adenoma of a bronchus the area of density in the roentgenogram is always much larger than can be explained by the extent of the tumor alone.

The major portion of the density revealed by the roentgenogram in almost all primary bronchial tumors results from atelectasis of the lung distal to the growth with or without associated infection. Occasionally either a benign or malignant bronchial tumor may be of such size and consistency that emphysema instead of atelectasis may be produced in the pulmonary tissues distal to the neoplasm. Unless infection is present in the lung distal to the growth, the roentgenoscopic findings of increased aeration on the affected side may be difficult to interpret, and usually the presence of neoplasm is not suspected.

The following case is reported because of the unusual combination of obstruction by cancer of the upper lobe of the left lung with atelectasis, and partial obstruction of the lower lobe on the same side with marked emphysema.

REPORT OF CASE

The patient, male, aged forty-four, was admitted to Medical College of Virginia Hospital on March 31, 1942. In March, 1941, he had had fever and cough which was productive of a small amount of purulent sputum. A roentgenogram of the thorax disclosed increased density in the upper two-thirds of the left lung (Fig. 1). Unresolved pneumonia was diagnosed, and the patient was given one of the sulfonamide drugs, with relief of symptoms. A month later another roentgenogram revealed marked decrease in the area of density.

The patient was then symptomatically well and continued with his work as a farmer until

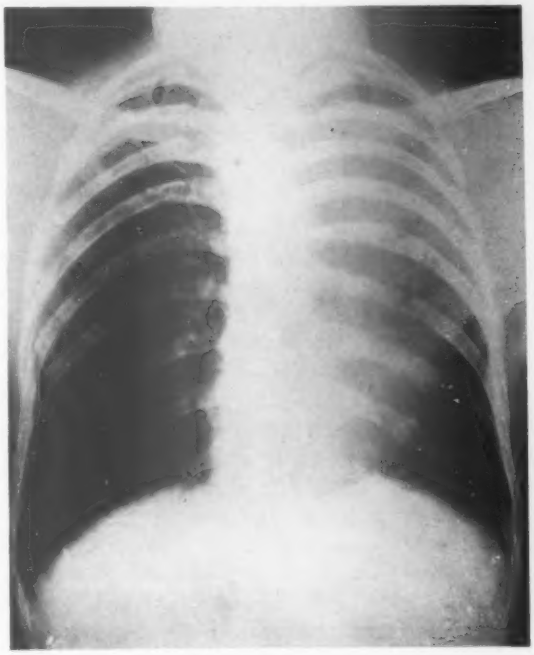

FIG. 1. Roentgenogram, March, 1941, showing density of upper two-thirds of left thorax.

the early part of March, 1942, when he noted cough, dyspnea, stridor, slight pain in the left side of the chest, and loss of weight. On examination the patient appeared a little anemic and he apparently had lost weight. General physical examination was essentially negative save for the findings related to the thorax.

The percussion note was normal throughout,

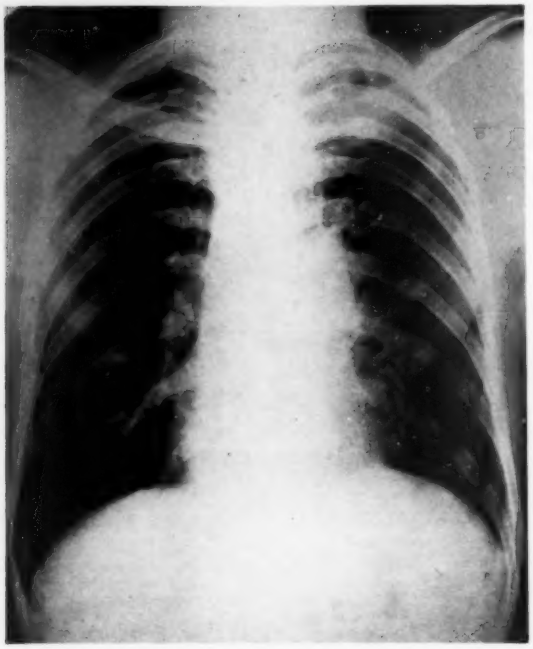

FIG. 2. Roentgenogram, March, 1942, showing apparent recession of density.

being equal on both sides, without evidence of displacement of the mediastinal structures. On the left side the breath sounds were inaudible, but on coughing and deep breathing there was definite stridor. Roentgenoscopic study of the thorax showed slightly increased density in the hilar shadows on the left side, but fairly normal aeration of the left lung (Fig. 2). Except for moderate secondary anemia, the laboratory studies revealed nothing significant.

The day after hospitalization bronchoscopic examination disclosed a large, pearly-white tumor in the left main bronchus, without evidence of associated infection. Large pieces of tissue were removed for microscopic study, which showed the tumor to be squamous cell epithelioma, Grade 2 (Fig. 3).

Although the tumor had apparently been present in the lung for more than a year, the patient's general condition was good, and surgical exploration was advised. Prior to operation a needle was inserted into the left pleural space, and manometric readings were plus 8 and minus 6.

Operation was performed April 8, 1942, under local and general anesthesia. When the pleura was incised, the left pleural space was found to be under considerable positive pressure and the lung protruded through the incision. The upper lobe of the left lung was completely atelectatic and occupied a small space in the anterior and medial portions of the mediastinum; the lower lobe was tremendously emphysematous and filled the remainder of the left portion of the thorax. In the region of the left hilum was a large mass of glands, and the growth was entirely inoperable. The wound was closed as an exploration. Postoperative convalescence was satisfactory, and the patient was dismissed from the hospital April 24, 1942.

FIG. 3. Photomicrograph of tissue removed at bronchoscopic examination.

SUMMARY

A case is presented in which a cancer arising in the bronchus to the upper lobe of the left lung had produced partial atelectasis of this lobe with roentgenoscopic evidence of increased density in the upper two-thirds of the left thorax. As the disease progressed, the left upper lobe bronchus became completely occluded, with total

atelectasis of the upper lobe of the left lung, and subsidence of symptoms for almost a year. Symptoms recurred with extension of the growth into the left main bronchus, the extension being of such character that it produced obstructive emphysema of the lower lobe of the left lung. Although the lesion had advanced to the stage of inoperability, the last roentgenogram, made a year after the original examination, suggested recession of the intrapulmonary disease.

TREATMENT OF POST-IRRADIATION ERYTHEMA WITH CHLOROPHYLL OINTMENT*

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CHLOROPHYLL, the green coloring matter in plants, is highly important in their metabolism. Chemically it belongs to the group of pigments, and is closely related to the porphyrines and hemins. It is the substance which transforms the sun rays into energy and acts, therefore, as the most vital catalyst in the biology of plants, and indirectly in the biology of animals. Its direct and indirect biological functions are manifold. Pharmacologically, chlorophyll plays a part in the metabolism of hemin, but an even greater part in its general effect on the organism of animals. As the carrier of the "energy of the sun" it has been thought to affect growth and the natural healing processes, although the exact fate of chlorophyll in human beings is still unknown. The possible use of chlorophyll in the treatment of the erythemas which follow radiation therapy was suggested to the authors by a paper by Gruskin[3] dealing with the therapeutic place of chlorophyll in acute and chronic suppurative diseases.

Gruskin reviewed 1,200 cases ranging from acute infections of the upper respiratory tract and the accessory sinuses to chronic ulcerative lesions of various types, especially those associated with varices, in which chlorophyll was the therapeutic agent used. He found it non-toxic whether taken by mouth in large amounts or given intravenously. Used externally in the treatment of two types of lesions (open wounds and deep infections with drainage tracts communicating with body cavities), it proved to be a safe, non-irritating agent, of distinct help in the treatment of wound suppuration. After its application, the character of the discharge changed, first becoming thinner and later of an almost watery consistency; healthy granulation tissue appeared, and prompt disappearance of the odor was noted. On freshly denuded surfaces, healthy granulations and wound healing were promoted and suppuration avoided. Even in cases of ulcerating cancer with putrefaction, chlorophyll tended to clear up the foul odor.

Wright[5] found chlorophyll in the form of ointment helpful in the treatment of chronic ulcers, especially those of the indolent, varicose type *In vitro*, chlorophyll had no definite bactericidal effect but it apparently has some bacteriostatic property. Wright attributed the clinical results to a highly complex process acting in part directly on the organisms themselves, and in part indirectly as a stimulant to cell metbaolism. The specificity of the bacteria present played no part, and it appeared likely therefore that the action of chlorophyll was biologic.

Bürgi[1,2] conducted extensive animal experiments on the effect of chlorophyll upon artificially produced wounds in guinea pigs and rabbits, comparing the effect on the healing of tissues with that of several other substances. Two wounds, 2 cm. in diameter, were made in each animal, one wound being covered with chlorophyll in the form of ointment and the other with the salve-base or with the material which was to be compared with chlorophyll. Bürgi found that chlorophyll caused faster healing than any other medication. During the healing process, the depth of the wound dried out, rich granulations grew promptly, particularly near the margins of the wound, the epithelium progressed forward from the margins rapidly, and the wound quickly became smaller; in other words, healing under chlorophyll treatment occurred in ten days without evidence of inflammation. Since

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chlorophyll is related to other vegetable products which have been used to promote wound healing, such as carotene, cod liver oil ointment, and vitamin A, Bürgi compared the healing properties of these substances with chlorophyll and found it definitely superior to any of the others. (This is interesting, especially in respect to vitamin A, because it has been called the epithelia-protecting vitamin.) In Bürgi's opinion chlorophyll has the properties of a vitamin, and he explains the granulation and epithelization as results of increased assimilation. He investigated different concentrations of chlorophyll, obtaining good results with concentrations of 2 to 10 per cent but finding even lesser concentrations effective. He warned, however, against higher concentrations, as two of his patients with varicose ulcers showed severe eczematous inflammatory reactions following highly concentrated chlorophyll applications.

MacKee[4] reported good results in the treatment of irradiation reactions with a jelly obtained from the plant *Aloe vera* which is found in Florida. The leaf of this plant is green and the jelly is obtained from between the outer and inner surfaces of the leaf. (We suggest that the effective element in this jelly is chlorophyll.)

These reports of the satisfactory use of chlorophyll in animal experiments and in conditions affecting human beings which are closely related to irradiation reactions led us to consider it as a therapeutic agent. It seemed possible that through its proper use the protracted period of healing of irradiation erythema could be shortened and secondary infection might be eliminated. Since irradiation reaction, including the physical discomfort of the patient, depends to a great extent on the presence of infection, its elimination would be an important factor; and in spite of the many treatments tried to achieve this end none, up to the present, has been successful. Theoretically, chlorophyll should relieve pain, lessen infection and shorten the time of healing; also by correctly timing its application, any denuding reaction may be avoided.

We began the use of chlorophyll in June, 1941, and have now treated 80 patients who had erythemas of varying degrees and at various sites. The majority of the lesions were located in the neck, the axilla, or the supraclavicular area. The fields ranged from 6 by 8 cm. to 15 by 15 cm., in some patients several fields being treated either at the same time or successively. The preceding dose of radiation varied from 1,500 r to 3,600 r, measured in air. The standard 200 kv. or 1,200 kv. technique was used. At first, the chlorophyll preparation was not applied until the erythema was fully developed, when the reaction was usually wet with beginning oozing and crusting and the patients were very uncomfortable. Later, the time of application was advanced to the appearance of the first sign of reaction. The chlorophyll was used either in the form of ointment or oil; both are easy to prepare and readily available. Following Gruskin's suggestion, an oil-soluble chlorophyll in a 3 per cent concentration, with a lanolin base for the ointment and peach kernel oil for the oil, was used. The best concentration of chlorophyll for clinical use has not yet been fully determined, but in none of our cases was any undue reaction produced by the 3 per cent concentration. In the beginning of our experiments a number of patients complained of a momentary, sharp burning, tingling sensation when the chlorophyll came into direct contact with the denuded and inflamed skin. The addition of 1 per cent nupercaine to the ointment and to the oil practically eliminated this unpleasant reaction.

Massachusetts General Hospital Prescription

OINTMENT CHLOROPHYLL

Chlorophyll (oil solub.)	3.0 gm.
Nupercaine, base	1.0 gm.
Petrolatum	30.0 gm.
Wool fat ad	100.0 gm.

Melt the wool fat and petrolatum at about 60° C. Dissolve the nupercaine in the melted wool fat mixture. When the nupercaine is completely dissolved, add the chlorophyll and stir until dissolved. Strain into container with loose fitting cover and sterilize at 20 lb. for thirty minutes. Allow to cool to approxi-

mately 60° C. and fill into previously sterilized collapsible tubes, under aseptic conditions.

Patients were instructed to apply the oil or ointment twice daily, covering the irradiated areas, and to continue as long as a definite reaction was present. It was discontinued when healing was complete.

RESULTS OF TREATMENT

As compared with vaseline or boric acid ointments the results following the use of chlorophyll appeared to be quite remarkable. Within a few days a distinct change was noticeable, the erythematous area was cleaner, the crusting had disappeared, the skin looked healthier, granulation appeared where the skin was denuded, and evidence of infection was absent. When infection had been present before the application of chlorophyll it disappeared. The patients felt more comfortable and did not complain of the burning, itching or soreness. There was no noticeable difference in the results of chlorophyll treatment with regard to the various voltages or filters used in the preceding irradiation.

A check-up examination of the patients two to four weeks later showed the healing process to be better than any we had previously obtained. As a rule the reaction subsided completely in two or three weeks, the new skin appearing smooth, pliable and pink.

Two patients who showed similar reactions at different sites were treated for comparison with chlorophyll and vaseline used simultaneously on separate lesions. This experiment was unsuccessful because both patients discontinued the use of vaseline when the better effect from chlorophyll became evident. Another patient, following 3,600 r to each side of his neck for carcinoma of the larynx, developed a rather marked erythema with epidermitis. Weeping, crusting, and desquamation of the skin with some ulceration had developed about two weeks after the termination of his treatment. There was an ill-defined collar of epidermitis anteriorly and laterally, and a few granulations at the margins of the skin. He was given chlorophyll oil to apply twice daily, at first experiencing only slight relief, but three weeks later the skin had healed completely and showed a soft, pinkish appearance.

In a very few instances we had an opportunity to use chlorophyll in long-standing irradiation ulcers. The reports of Gruskin and Bürgi on indolent varicose ulcers led us to try it for this type of ulceration which does not respond readily to conservative therapy. One patient, following the application of 5,000 r to one side of the neck, given in daily doses of about 300 r each, developed induration of the deep layers of the skin six weeks later, with a sluggish, painless ulcer, measuring 2 by 3 cm., covered with a crust, in the center of the treated area. After the application of chlorophyll the character of the ulcer changed; the infection cleared up and healing occurred in four weeks. In another patient with a deep irradiation ulcer behind the ear, some improvement was apparent after the fourth chlorophyll treatment. In general, however, the result of this treatment in long-standing ulcers has been disappointing.

In one patient only, reaction to chlorophyll treatment, characterized by redness, swelling and edema, occurred. It subsided promptly after the ointment was discontinued, and was attributed to hypersensitivity to nupercaine.

There appeared to be no difference in the results of ointment and of oil. The choice between the two depends solely on convenience of application—each is easy to apply. Recently the ointment has been in general use for out-patients. The treated areas in either case should be covered with gauze to prevent chafing.

Summarizing the results of our experiments, we agree with Gruskin and Bürgi that a biologic factor plays a part in the vitalizing effect of chlorophyll and may explain its superiority to other substances previously tried. Our limited experience does not warrant drawing more than tentative conclusions, but since our results duplicate those of Gruskin and Bürgi in

related conditions we feel justified in recommending the use of chlorophyll. In our group of patients chlorophyll, associated with good nursing and after-care, sometimes neglected but very essential to these patients, has accomplished more than any other method we have tried. It has kept the patients fairly comfortable at a time when the irradiation reaction would normally cause considerable discomfort. As a matter of fact, we have rarely had an opportunity to see a severe irradiation reaction since we began the use of chlorophyll early and routinely. The length of the reaction has been shortened and healing accelerated; infection has been avoided and granulation and epithelization have been rapid. Each of these factors contributes much to the relief of the patient, and is therefore of double value.

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THE TUBERCULOSIS CONTROL PROGRAM OF THE UNITED STATES PUBLIC HEALTH SERVICE*

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FOR the first time in this generation, the forces fighting tuberculosis in the United States appear to be in danger of a setback. It seems likely that the battle, which has been attended by steady success for the last twenty-five years, may now take an unfavorable turn. The most hopeful observers look for a leveling off in the tuberculosis mortality rate—a sort of stalemate between the opposing forces. Others fear that the hitherto declining mortality curve is about to rise.

The reason for this gloomy outlook, of course, is the war. The intimate relationship between war and disease is manifested with particular emphasis in the case of tuberculosis. The last world conflict sent tuberculosis rates skyward in the nations of Europe and brought an increase in tuberculosis deaths in this country. Today alarming increases are again being noted throughout Europe, and no one can tell how extensive the damage will be.

Although there has been no apparent increase in the amount of tuberculosis in this country, the objective circumstances favoring such an increase are much in evidence. Unless prompt and effective counter measures are taken, these influences will certainly be reflected in the statistical tables which are the communiques from the tuberculosis front.

Notable among the factors aggravating the situation are:

1. Large concentrations of industrial workers and their families, many of them in communities without proper housing, sanitation, public health, or medical facilities.

2. The fatigue resulting from the increased hours and tempo of work demanded to keep the war machine going.

3. The employment in industry of thousands of women and others unaccustomed to heavy work, including many with minimal or inactive tuberculosis who will break down or become reactivated under the strain of the job.

Even if America is fortunate enough to escape the devastation and disease which would result from the clash of armies upon its soil, these wartime circumstances and conditions are sure to exact a toll in ill health and physical disability.

Yet America cannot afford ill health or disability. Today, when every last ounce of energy is needed to defeat an enemy who is strong, determined and ruthless, avoidable illness becomes a threat to our very existence as a nation.

Tuberculosis, however, does cause ill health and disability. Those it generally strikes down are the very ones who are most valuable as fighters and workers—men and women between the ages of twenty and fifty. When protected from the disease these individuals are the human assets upon which the presumption of victory is based. When attacked by the disease they become liabilities who spread sickness to others and who require time and money and services which could otherwise be used for prosecution of war.

Faced with these two contradictory factors—the increased opportunity for the spread of tuberculosis and the necessity of conserving human resources—only one reasonable course can be taken. There must be a redoubling of effort to maintain and extend a balanced, effective tuberculosis control program.

A balanced program is based on the following cardinal principles of public health practice:

* Presented at the Forty-third Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 15–18, 1942.

1. Find tuberculosis early.
2. Provide isolation and treatment through sanatorium and medical care.
3. Promote after-care and rehabilitation.
4. Support research in new methods of control.
5. Employ every available means of public health education.

Application of any of these principles without the others means something short of success.

In addition to preserving nutritional standards, maintaining personal hygiene, and improving housing facilities—general measures which affect all of the people—there are certain specific things that should be done immediately to control tuberculosis. The United States Public Health Service, recognizing this threat to the health of the nation, established an office of Tuberculosis Control in the States Relations Division shortly after war was declared.

The objectives of the Office of Tuberculosis Control have been defined as follows:

1. Widespread chest roentgenologic examination of workers in war industries.
2. Chest roentgen examination and public health education of families in war industry communities, and especially of minority and underprivileged groups.
3. Extension of the chest roentgenologic examination procedures of the Army and Navy to Coast Guard recruits.
4. Elaboration of a workable system, in cooperation with Selective Service, the Army, Navy, Coast Guard, and state health departments, for immediate reporting to state and city health departments of all recruits rejected because of tuberculosis. This would result in full advantage being taken of the case-finding being done by the medical corps of the armed forces.
5. Tuberculosis consultation service to state health departments upon request, with a view to rapid inventory and reorganization of control programs on a war-time basis.

(a) Plan for coordination of the efforts of official and voluntary agencies on a state level to avoid duplication and to concentrate power.

(b) Accumulate current information on basic needs of each state so that a framework can be formed upon which to build a sound structure for tuberculosis control when the emergency is over.

The Office of Tuberculosis Control, in cooperation with the Division of Industrial Hygiene of the National Institute of Health, has provided portable 35 mm. roentgen-ray service for war industries in order to stimulate mass chest roentgen examination of defense workers. Whenever possible, industrial establishments are encouraged to procure their own equipment and personnel, using all available methods of roentgen examination.

The photofluorographic units, consisting of a medical officer, technician, clerk, and full equipment for taking and processing 35 mm. films, are loaned to state health departments for limited periods to be used in examination of large industrial groups. The resulting surveys afford a demonstration of the need for mass case-finding in industry and provide a means of training additional personnel who will be ready when the states can procure their own equipment. Eight of the units are in use in various states and are available to others in the order in which requests are made. With good cooperation and teamwork, 300 to 500 workers can be examined in one working day.

Thirty-five millimeter chest roentgen films are used by the Public Health Service in surveys of war workers and Coast Guard recruits because it is felt that they provide a satisfactory method of quickly and economically finding the vast majority of significant cases of tuberculosis in large population groups.

Experience in Minnesota and Washington, D. C., has demonstrated that less than 10 per cent of minimal lesions are missed by this method. Advanced lesions are detected just as accurately as with 14×17 inch roentgen films.

If all cases of tuberculosis in this country,

except 10 per cent of the minimal cases, could be discovered the control of this disease would be a simple matter. As a matter of fact, one-third of the so-called minimal cases, discovered by roentgen examination, are inactive when studied clinically, and an additional one-third are questionably tuberculous because the clinical findings do not warrant anything but an indeterminate diagnosis. So the actual proportion of undetected significant minimal lesions is closer to 3 per cent than 10 per cent. This amount is not of much importance from an epidemiological point of view.

It should be pointed out that the task of the Public Health Service is to protect the public health to the fullest extent possible with the funds appropriated by your Government for that express purpose.

An important part of the protection of the public health is the control of tuberculosis. This is a recognized public responsibility. Early diagnosis of this communicable disease is dependent upon roentgen examination of the chests of the greatest possible number of people. With the limited resources available to us for this purpose, sound scientific judgment dictates that the method used must be one which benefits the group rather than the individual. Until such time as you roentgenologists and other public spirited citizens make yourselves heard in your demand for nothing but the best—in this case, high-quality 14×17 inch celluloid films, interpreted by experts—we will try to do the best we can with what we have.

In the fight to conserve man power for war production, tuberculosis is an insidious enemy worthy of consideration. It affects 1 per cent of our man power and may affect more if its prevalence increases, and if its communicability makes itself felt not only among other workers but also in the home. Time is tremendously important, and the private practitioner can not do enough mass roentgenologic surveys to affect noticeably the total group involved.

This attitude, however, does not detract from the intrinsic value of the interpretation of individual films by roentgenologists, who are truly experts in their field.

The processed roentgen film itself is not relatively expensive, but interpretation has been and undoubtedly will continue to be the more costly part of the total examination when done by specialists. There has been considerable confusion regarding cost of film and cost of interpretation, especially in the minds of lay people. It is your responsibility, more than that of any other group of practitioners, to dispel this confusion. We will do our part by limiting the use of 35 mm. roentgen films to screening out abnormal and suspected lesions which can be confirmed or denied by means of 14×17 inch films interpretated by experts in this field.

In developing a program of tuberculosis control in any community, the cooperation of state and local medical societies, industrial mangement and labor representatives, and voluntary agencies is solicited. Such cooperation is essential in order to insure success of the program and appropriate therapeutic treatment and after-care.

Obviously, the redoubling of effort necessary to keep tuberculosis in check during this national crisis will require the fullest degree of cooperation among all official and voluntary agencies concerned with the problem. Each type of agency must recognize the particular responsibilities and limitations of the other. Since it is a wartime program, the methods and purposes of which must be coordinated with other aspects of the total war effort, the responsibility of the Government for over-all planning and coordination is well recognized.

The forces arrayed against tuberculosis in this country now face their supreme test. The experience gained in twenty-five years of constant battle must now be utilized for a smashing blow against an enemy who has suddenly been greatly reinforced. This experience is sufficient to guarantee victory, but increased tempo of the battle makes the deployment of new forces imperative and

the urgency of the situation calls for new tactics.

If our tuberculosis forces fail to hold their ground now it will be because they do not translate their experience and knowledge into achievement. If they stand firm, permitting no depredation of our manpower, they will make a great contribution to winning the war.

DISCUSSION

Dr. John H. Harris, Harrisburg, Pa. I should like to ask the speaker if it is the intention of the Public Health Service to make these surveys of industry without cost to the industry.

Dr. Francis F. Borzell, Philadelphia. I should like to ask Dr. Hilleboe to explain, if possible, the method of cooperation with the local radiologist in these industrial surveys, because of the fact that eventually the patient becomes a local problem, and it would seem to me from past experience that there has not been an attempt to enter into a community with proper preparation in the matter of coordination with the local radiologist who will have the problems after the survey has been made.

Dr. Hilleboe (closing). In reply to Dr. Harris' question which was as to whether or not any charge is made to the industry, I did not point out that these units are not handled direct from Washington, but are loaned to the state health department and are operated as a part of the state health department set-up. In other words, it may be the Division of Tuberculosis Control in the state or the Industrial Hygiene Division in the state.

There is no requirement from Washington as to any charge to industry, and in the majority of instances so far it is my knowledge that the state health departments are not making any charge to industry for this service. I think there is a reason for that and a reasonable one. In those instances where there are insufficient facilities or no facilities for roentgen examination of the chest, one of the difficulties has been that industry, particularly management, does not feel that this work is necessary, so the state health department, through its industrial hygiene division, attempts to show, on a demonstration basis, what can be done by mass roentgen examination of industry.

I want you to appreciate that this is not a continuous service which is given for an indefinite period of time. It is given to a particular industry in order to show what can be done. For example, in the New York Shipbuilding Corporation, in Camden, New Jersey, there is a regular medical staff. Preëmployment examinations are made by the regular staff with consulting roentgenologist and tuberculosis specialists entering into the picture. However, there happen to be, as you might expect, many thousands of workers in this defense or war industry, and management did not feel that it had the time or could spend the money to go through this entire group and find out what the situation was. Actually, it is of little importance to examine just those coming in, if you know nothing about the large group of people working in the industry. So in this particular instance, at the request of the State Board of Health of New Jersey, we loaned a unit for the purpose of making examinations of the industrial workers in this war industry.

In regard to the second question as to whether or not there is cooperation with the local radiologist and the question of coordination with local people, I am sure you gentlemen appreciate that the diagnosis of tuberculosis is only one part of the whole problem. We must provide medical care. We must provide sanatorium care. There is the question of after-care and rehabilitation of these people, and I think that we should point out also that the roentgen diagnosis is just the preliminary step. We have learned recently from the examination of the young men coming into the induction centers that an outright diagnosis of tuberculosis as a cause for rejection causes great hardship to the individual selectee who is rejected because, in a considerable number of cases, the tuberculosis is of the type that we commonly refer to as first infection and is of no particular clinical significance. In regard to control of the disease, it is quite essential to follow through this roentgen examination by proper clinical study to determine, on the basis of differential diagnosis, whether or not the lesion is one which can be called tuberculosis and, second, whether or not there is evidence of activity sufficient to require sanatorium or medical care. We work very closely with the local health department and do not supervise the units direct from Washington, except through the state health departments.

As soon as a person who has tuberculosis is

found by means of one of these surveys, that person is handled in exactly the same way as any other person found to have tuberculosis in the community would be handled. That means that in some communities radiologists are brought into the picture, where radiologists are in the tuberculosis picture in that community. In other communities tuberculosis specialists are brought in perhaps before the radiologists, but every effort is made to bring everyone in, in the local community, who is concerned with tuberculosis.

I pointed out in my few brief remarks that we do not proceed with one of these projects on a state level until the state health department has definitely worked out cooperative arrangements with the medical societies, and certainly you gentlemen are represented there, with management, with labor, and with the voluntary tuberculosis associations. As long as those precepts are followed everyone will benefit from this type of case-finding and follow-up program for the control of this communicable disease.

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THE DIAGNOSIS OF CERVICAL METASTASIS FROM SQUAMOUS CARCINOMA OF THE MOUTH AND THROAT

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THE management of metastasis to the cervical lymph nodes plays a part in the treatment of every squamous carcinoma of the face, mouth, and throat. Since squamous carcinoma of these regions makes up a large part of the number of accessible cancers, the roentgenologist is confronted every day by some aspect of the management of cervical metastasis. Of the various aspects, that of making a diagnosis is the simplest and one which does not depend for its success on any advance in our present knowledge of cancer.

PHYSICAL DIAGNOSIS OF CERVICAL METASTASIS

The physical diagnosis of metastatic squamous carcinoma of the cervical lymph nodes depends upon the discovery of a primary cancer and the presence of a particular kind of regional adenopathy. The adenopathy must have all of the following characteristics: recent origin, a firm consistency, a lack of tenderness, and a history of progressive enlargement. The absence of any one of these characteristics throws doubt on the accuracy of the clinical diagnosis.

For purposes of treatment, the diagnosis of metastasis is incomplete without a knowledge of the number and the position of all metastatic nodes. Primary cancer of the face, mouth, and throat each has a more or less characteristic metastatic pattern. Most patients have only one metastatic node which, if secondary to a differentiated primary squamous carcinoma, may reach a diameter of several centimeters. Some patients have two nodes, but the presence of more than two nodes on one side of the neck is unusual with squamous carcinoma of the mouth, lip, and face. When multiple unilateral metastases are present, they decrease in size from top to bottom because the cervical lymph nodes form vertical chains and because the cancer cells pass downward from node to node.

The position of the first adenopathy is an important point in the clinical diagnosis of metastasis (Fig. 1). With rare exception, the first lymph node enlarged by the growth of metastatic cancer cells must be that one of the cervical chain which is nearest the primary cancer. If the first cervical mass is not in this typical position, it is a good practice to defer a diagnosis of metastasis until the examination of a biopsy specimen is reported. An atypical position of a suspected metastasis suggests one of the following conditions: some other type of adenopathy, a primary tumor of the neck, metastasis from a squamous carcinoma of unusually high malignancy, or a metastasis from a second primary squamous carcinoma.

Confinement of the metastasis to a few cervical nodes in the upper half of the neck is a striking characteristic of squamous carcinoma of the face and mouth. Except in hopelessly advanced cases, visceral metastases are distinctly uncommon. A roentgen examination of the chest is not usually indicated to exclude metastasis of the lungs, the commonest type of visceral metastasis. I have seen one case, however, in which microscopic examination of autopsy tissues showed visceral metastases, although there was no cervical metastasis.

In the majority of patients, the clinical course of metastasis of the neck is consistent with and the basis of the belief that cancer cells always reach the nodes as emboli, none remaining or growing in the lymph vessels. Except in very rare cases of

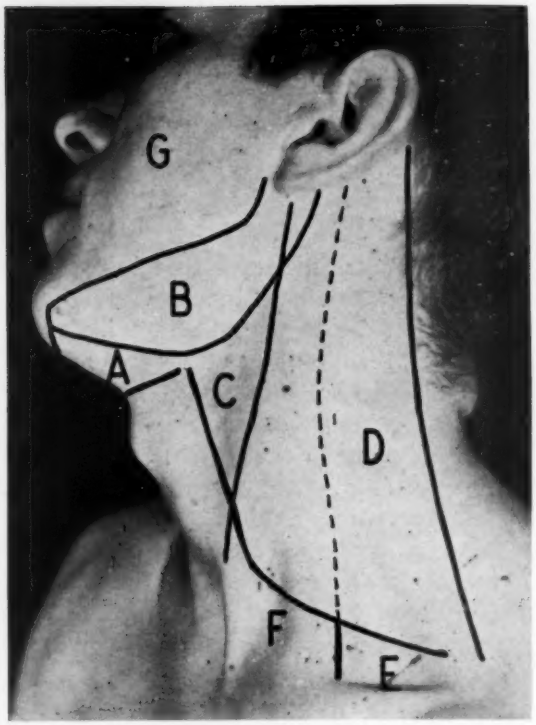

FIG. 1. Anatomical triangles of the neck. The position of the first metastasis from squamous carcinoma of various tissues of the head and neck. A clinical diagnosis of metastasis is seldom correct if a mass in the neck is not regional to the site of the primary neoplasm.

	Name of Triangle	Approximate Frequency of Occurrence of First Metastatic Node in Various Triangles	Site of Primary Squamous Carcinoma Which Metastasizes First to This Triangle
A	Submental	1– 2%	Lip, chin, anterior part floor of mouth
B	Submaxillary	60–80%	Any part of mouth, face, lip, antrum
C	Carotid	20–30%	Any part of pharynx, tonsil, base of tongue
D	Occipital	–1%	Skin overlying the triangle, scalp
E	Subclavian	–1%	Skin of upper extremity—particularly hand—(breast; on left, thorax and abdomen)
F	Muscular	3– 5%	Larynx—particularly extrinsic type, esophagus, rarely tip of tongue
G	Buccal nodes	–1%	Nasal vestibule; adjacent skin

permeation of the lymphatics of the neck with physical signs like those of the en cuirass type of breast cancer, participation of the lymphatic vessels cannot be diagnosed by physical examination or any other kind of clinical examination. But is it safe to accept the absence of physical signs as proof of the complete absence of cancer cells in the lymph vessels? In the presence of metastatic nodes, should not the vessels always be treated for cancer?

It seems reasonable to suppose that if a microscopic examination were made of all lymphatic structures of the neck in various clinical types of metastasis, examples of all degrees of involvement of the lymph vessels would be found from no cells to complete permeation, and further to suspect that the degree of lymph vessel involvement found in a particular case of metastasis would correspond more or less exactly to the growth characteristics of the cancer cells of the associated primary malignancy. Some cases classed by physical examination as having "ruptured capsule" and "infiltrating metastasis" might prove to be cases of permeation of the lymph vessels, if all the lymphatic structures of the neck were examined microscopically.

According to this hypothesis regarding the extent of involvement of the lymph vessels, the physical findings in the average case of metastasis, namely a single metastatic node, would be explained by the low grade malignancy of the primary tumor. The accepted surgical treatment of cervical metastasis, namely, the dissection of lymph vessels and nodes rather than the local excision of the metastatic nodes alone, is based on the belief that cancer in the nodes means probable cancer in the vessels. This belief would seem to be equally applicable

to treatment by irradiation. Whatever the method of treatment, irradiation or surgery, the same size of treatment field must be used, and the field must be big enough to include the normal lymph node of the cervical chain below the lowest clinical metastasis and the intervening lymph vessels. Thus, roentgen rays must be used to treat viable cancer which may be in the lymphatic vessels if the nodes have been implanted with radon seeds.

However, in order to save the skin from the backscatter effect and to avoid constitutional reactions, one is advised to use the smallest treatment field consistent with the extent of the disease. Adjustment of the factors of roentgen treatment to preserve the skin overlying the metastasis reduces the roentgen-ray dosage to a fraction of the dosage of radiation, derived from radium and roentgen rays, which is given accessible primary cancer that grows from a surface which is intentionally destroyed by treatment. The smaller roentgen-ray dosage of the metastasis appears to be one reason for the apparently greater radioresistance of the cancer cells in the lymph nodes. A higher degree of malignancy of the cell of a metastasizing cancer may be another reason for greater radioresistance. Since metastasis is the cardinal sign of malignancy, a squamous carcinoma which produces metastasis is a more malignant tumor, in the biological sense, than one which never metastasizes, and the cells of such a cancer which reach the nodes may, for this reason, be more difficult to destroy than the cells of a non-metastasizing primary cancer.

In this era of carcinogens and cyclotrons, it is easy to overlook the value of the simple lessons learned in the early days of cancer care. One such lesson concerns the value of physical examination in diagnosis and prognosis. In spite of advance in treatment, physical examination must still be depended upon to detect the loss of mobility and of the sensation of capsule which indicates invasion of the surrounding tissue by cancer cells of the metastatic nodes. A small Stage II metastasis (the operable, movable, or non-infiltrating type) imparts to the encircling fingers, if the surrounding muscles are relaxed, the sensation of a movable ball, but the mobility of this type of metastasis is also determined by its size and position. If large, the mobility of a metastatic node is limited by the completeness with which it fills the surrounding space and the extent to which it stretches the overlying sternomastoid muscle and deep cervical fascia. Stage III metastases (the inoperable, immovable, and infiltrating type) are not always large, and at times they do not feel at all like nodes but like a cellulitis. This diffuse thickening and induration of the tissues about a node is a physical sign of the most malignant type of metastatic node. The high grade of malignancy rather than any lack of therapeutic skill explains the frequent failure of surgical and radiation treatment to control this infiltrating type of metastasis.

That the center of large nodes is occupied by gray, flocculent fluid, is easily proved by aspiration. The escape or absorption of this fluid causes noticeable shrinkage of the metastasis If such shrinkage occurs during roentgen treatment, it may be attributed erroneously to the destruction of the cancer cells. Fluid may play another part in treatment. A large amount interferes with the accuracy of spacing of implanted radon seeds. If the point of the implanters enters the fluid, the seeds will fall through the fluid and collect at the lowest point of the cavity, thus preventing uniform irradiation of the node.

DIFFERENTIAL DIAGNOSIS OF CERVICAL METASTASIS

A mass which is found in the neck of a patient with cancer of the mouth is not necessarily a metastasis. A mass resembling a metastasis may be produced by obstruction of the duct of a salivary gland, by invasion of the tissues of the neck by a primary cancer, and by chronic cellulitis of the neck tissues. Either Stensen's duct or Wharton's duct may be obstructed by in-

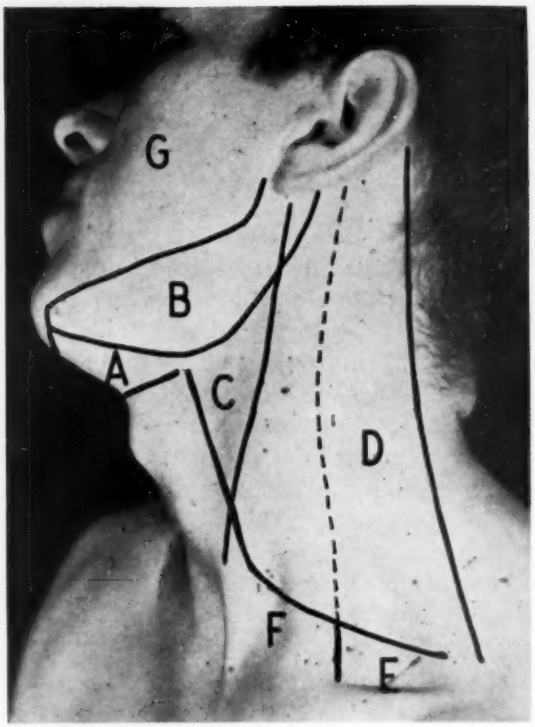

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Fig. 2. Mass resembling a lymph node metastasis of squamous carcinoma. Enlargement of the submaxillary salivary gland resulting from invasion of Wharton's duct by a squamous carcinoma of the mucosa of the floor of the mouth.

vasion of the primary cancer or by scar tissue resulting from treatment. Such obstructions cause an enlargement of the salivary glands from retention of saliva or a chronic adenitis which must be differentiated from a metastasis (Fig. 2). The infiltrating type of squamous carcinoma originating in the mucosa of the floor of the mouth or the tonsillar fossa may destroy the thin mylohyoid or superior constrictor muscle and invade the tissues of the submaxillary (Fig. 3) or the parotid

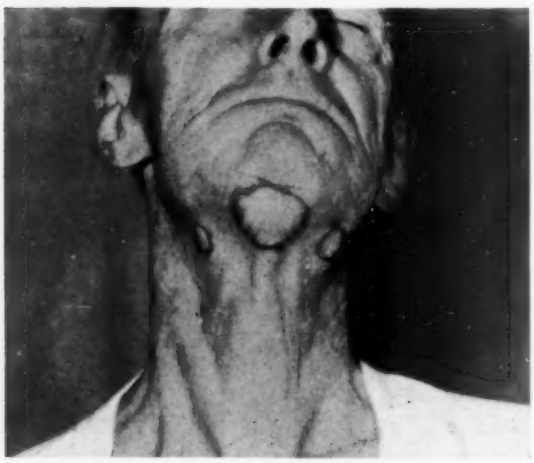

Fig. 3. Mass resembling a lymph node metastasis of squamous carcinoma. Invasion of the soft tissues below the chin (submental region) by a squamous carcinoma of the mucosa of the floor of the mouth.

space, thus producing another kind of upper neck mass resembling metastases. Furthermore, therapeutic destruction of such an infiltrating primary cancer may produce a fistula through which mouth bacteria enter the neck and cause a confusing mass of inflammatory tissue (Fig. 4). The true nature of any of these kinds of neck mass cannot be learned by physical examination because they have the same physical characteristics as Stage II or Stage III metastases. Diagnosis of such masses of the neck can be made only by

Fig. 4. Mass resembling a lymph node metastasis of squamous carcinoma. Brawny induration of the entire left side of the neck resembling permeation of the lymph vessels by carcinoma, but due to an abscess complicating a "transitional cell carcinoma, Grade 3" of the left tonsil.

the microscopic examination of a biopsy specimen. Without a microscopic diagnosis one may abandon irradiation because an inflammatory mass is mistaken for a hopeless metastasis, or improvement of an inflammatory mass during irradiation may create a false impression of the effectiveness of treatment.

The commonest error in differential diagnosis consists in regarding small, multiple, non-neoplastic nodes as metastases (Fig. 5). Both the benign and the malignant adenopathy of this type occur in younger cancer

patients whose lymphoid tissues have not yet undergone senile atrophy. Although the non-neoplastic nodes are usually the softer, smaller, more numerous, and more scattered of the two kinds, the clinical diagnosis is not always easy. Moreover, there is a very malignant type of metastasis which has the same physical characteristics (Fig. 6). Insofar as the differential diagnosis can be made by physical examination one must use the character of the primary cancer to distinguish the two types, but an examination of a biopsy specimen is always necessary for final diagnosis. Small metastatic nodes can escape detection because they are covered by a thick layer of subcutaneous fat (a short fat neck), by a radiation edema of the tissues of the suprahyoid region, by the parotid gland, or by the lower half of the sternomastoid muscle.

Obviously a diagnosis of metastasis is a contradiction of terms until the primary

Fig. 5. Mass resembling a lymph node metastasis of squamous carcinoma. Non-neoplastic adenopathy of the left submaxillary region associated with an infiltrating squamous carcinoma of the lip.

Fig. 6. Multiple cervical metastasis from a "carcinoma of the Schneiderian membrane" of the left ethmoid region resembling in number and distribution non-neoplastic adenopathy.

Fig. 7. Mass resembling a lymph node metastasis of squamous carcinoma. The final diagnosis was squamous carcinoma, Grade 4, of a branchial cleft remnant.

FIG. 8. Mass resembling a lymph node metastasis of squamous carcinoma. Referred as a cancer of the right tonsil with cervical metastasis. Diagnosis: "Mixed cell tumor" of parotid gland occupying the pterygomaxillary and submaxillary fossae.

cancer is found, but detection is not always easy. In fact, in a small percentage of cases with nodes in the neck which eventually prove to be metastatic squamous carcinoma, a primary cancer is never found by physical examination. Even after an autopsy one will sometimes have difficulty in deciding whether such a cervical mass is a metastasis or a primary squamous carcinoma of the neck. Such a dilemma, namely, no primary cancer and squamous carcinoma in what appears to have been a cervical node (the normal architecture of the lymph node is lost in a large metastasis), is usually explained as squamous carcinoma of a branchial cyst remnant (Fig. 7). Such a clinical situation creates a real problem in the diagnosis of metastasis.

Usually, examination of a biopsy specimen of a suspicious neck mass not associated with a primary neoplasm will not show squamous carcinoma but some other tumor. Carcinoma and mixed tumor of the submaxillary salivary gland (Fig. 8 and 9), primary sarcoma of the lymph node, carotid body tumor, aberrant thyroid tissue, Hodgkin's disease, and even fibrous tuberculosis of the node may be confused with squamous metastasis, if no primary cancer is found.

Although there is usually little doubt in an examiner's mind regarding the malignant nature of a primary growth or even of the histopathological type of malignancy of primary growths arising in or about the mouth, since most are squamous carcinoma, all agree that a biopsy specimen should be taken from the primary growth to guard, for the patient's sake, against every possible error in diagnosis and to furnish the physician with material for the scientific study of cancer. For these same reasons, should not biopsy specimens also be taken from enlarged nodes? Yet, contrary to expectation, radiotherapists, with the exception of Martin and Ellis[4] do not advise the removal of a biopsy specimen, and appear to depend solely upon clinical examination for the diagnosis of cervical metastasis. It is granted that the error in clinical diagnosis of large metastatic nodes is low, but it should be emphasized

FIG. 9. Same patient as in Figure 8. Apparent neoplasm of the right tonsil due to the inward displacement of the wall of the oropharynx produced by the mixed cell tumor of the deep surface of the parotid gland.

that the diagnosis of small nodes is inaccurate to a surprising degree. The frequency of error in the clinical diagnosis of small nodes found by the microscopic examination of surgical dissection specimens is reported by others as follows:

1. One-half of 326 specimens from patients operated upon for metastatic squamous carcinoma contained no cancer.
2. One-third of the specimens from 148 prophylactic operations did contain cancer.

One suspects that a knowledge of these errors in diagnosis explains the routine performance of prophylactic neck dissections in some good surgical clinics. In spite of the difficulty in making a correct diagnosis of small metastatic nodes, neck dissection or radiation treatment is not necessary if on admission no nodes are felt. Routine prophylactic treatment presumes that metastasis will occur in all patients. Compilation of figures published by others actually shows, not 100 per cent of metastasis, but the following percentage of metastasis (total percentage on admission and after treatment of the primary cancer) from primary squamous carcinoma from various anatomical sites: lip, 26.5 per cent (2,305 cases); mouth, 41.9 per cent (2,275 cases); throat, 69.5 per cent (865 cases). Stating these findings in another way, and in round figures, metastasis does not occur in 75 per cent of cases of cancer of the lip, 50 per cent of cases of cancer of the mouth, and 25 per cent of cases of cancer of the throat.

The frequency of metastasis which appears after the treatment of primary cancer has, however, a much more important bearing on the question of prophylactic treatment. In this type of case, the incidence of metastasis is also far from 100 per cent. In a large series of patients followed for five years, Martin and his associates found the incidence of metastasis after treatment of the primary cancer to be 12 per cent in cancer of the lip,[5] 40 per cent in cancer of the tongue,[6] 3 per cent in cancer of the tonsil,[7] and 17 per cent in nasopharyngeal cancer.[3]

When the physical examination shows an obvious metastatic node, what is the probability of the presence of cancer in neighboring nodes which are too small to be felt? Unless one disregards the extent of metastasis and treats in the same way the side of the neck, or both sides of the neck, of all patients with cancer of the mouth, one needs this information as a guide to the width of the margin of apparently normal tissue surrounding a metastatic node which must be included in the treatment field. In search of an answer to this question, I examined 45 surgical neck dissection specimens. A total of 99 metastatic nodes had been found during the physical examination of these 45 patients. The microscopic examination of the nodes of all the neck dissection specimens showed a total of 110 metastatic nodes, 11 more than were found by physical examination. Only 2 of the 11 additional metastatic nodes found by microscopic examination occurred in Stage II node cases.

These figures create the following impression: When metastatic nodes are of the operable type, all metastatic nodes can be felt. The confinement of metastatic cancer to palpably enlarged nodes in most of these 45 patients should not be used, however, as an argument for local treatment of the enlarged nodes alone, either by excision or implantation of radon seeds, but these findings appear to furnish an explanation of the successful use of seeds in the control of the metastatic process in those cases where implantation of the palpable nodes with radon seeds has been the only treatment of any kind for metastatic cancer of the neck. The tendency of slowly growing cancer to remain confined to one node also appears to explain control of metastasis from cancer of the larynx by neck dissection. Cells from cancer of the mouth must pass through three or four lymph nodes before reaching the thoracic duct. For this reason, cancer of the mouth offers the physician a much better opportunity to remove all cancer of the neck with a margin of normal tissue (lymph nodes and lymph vessels nearer the chest than the lowest metastatic node) than

cancer of the larynyx which is separated from the thoracic duct by only one or two nodes.

Clinical diagnosis, which consists of the history, local examination, and general physical examination, was formerly the physician's principal means of determining the diagnosis and prognosis of cancer. Today the physician is too apt to act as though the microscopic grade of a squamous carcinoma summarized all the prognostic data of any importance and to accept the microscopic grade in preference to conflicting clinical evidence. This is unwise as the course of the individual cancer will often prove that the prognostic impression derived from clinical examination is more correct than the conclusion from grading alone.

Much can be learned from the physical examination of the metastasis. At a glance, some metastases and some types of metastasis can be classified as incurable, whatever the microscopic grade. Insofar as physical examination of metastatic nodes alone has prognostic significance, the discovery of a single small metastatic node immediately places the case in the group of more malignant primary cancers. The following physical findings are reliable signs of a high degree of malignancy of the metastasis and a bad prognosis: (1) metastasis from an undiscovered primary cancer; (2) atypical position of the first metastatic node; (3) large size of the metastatic node; (4) rapid growth of the metastatic node; (5) numerous unilateral metastases; (6) cross metastases (appearing in the side opposite to that of the primary cancer); (7) infiltrating and ulcerating metastasis. A short, latent period—time interval between the appearance of the primary cancer and that of the metastasis—has the same meaning.

MICROSCOPIC DIAGNOSIS OF CERVICAL METASTASIS

A microscopic examination is needed to confirm or correct the clinical diagnosis of metastasis and to classify squamous carcinomata according to the degree of differentiation.

It is the duty of the clinician to provide the pathologist with a biopsy specimen adequate to furnish the information desired. The pathologist should not be forced by an inadequate specimen to give an indefinite report. An adequate specimen and an accurate diagnosis of small metastatic nodes is unduly important because this is the only type of metastasis in which lasting control can be expected with any degree of confidence. If the clinician wished to know only if a neck node is malignant or benign, the small fragments removed by aspiration through a needle may be adequate, but only if one has been fortunate in the placement of the needle point, and if the pathologist has taken the trouble to train himself to interpret the nature of changes in single cells or very small pieces of tissue. Needle aspiration of biopsy specimens is popular with clinicians because of the simple technique, and it appeals to some patients because it avoids a surgical incision, but it places upon the pathologist a responsibility for which he may be unprepared or one which he is unwilling to assume. There are two very common non-malignant conditions of regional lymph nodes, namely: sinus catarrh and reticulosis which can furnish epithelioid cells that may be confused in needle aspiration biopsy specimens with the epithelial cells of squamous carcinoma.

Instead of these tissue fragments, one can remove a solid core of tissue with the same simple technique by substituting the Silverman needle (Fig. 10) for the needle and syringe. The core of tissue obtained by the Silverman needle will provide a microscopic section which the pathologist of average experience in tumor diagnosis may find adequate for accurate diagnosis and even cancer grading, but it is not so well suited for rapid diagnosis by the smearing and staining technique of Martin and Ellis,[4] a technique which resembles the preparation of a blood smear. If the clinician wishes to be sure of the grade as well as the presence of

squamous carcinoma in the nodes, he must secure a node or a large piece of a node and finally, if the clinician is interested not in the mere presence and grade of the metastatic cancer, but in the entire pathologic findings of cervical metastasis which includes the changes in the lymph vessels in addition to neoplastic and non-neoplastic tumor metastasis can explain some unexpectedly good responses to irradiation.

Cancers are not graded by nature but by a pathologist. The clinician is apt to forget that although the actual microscopic section may show any one of the many degrees of anaplasia, a pathologist must phrase his conclusions in a few arbi-

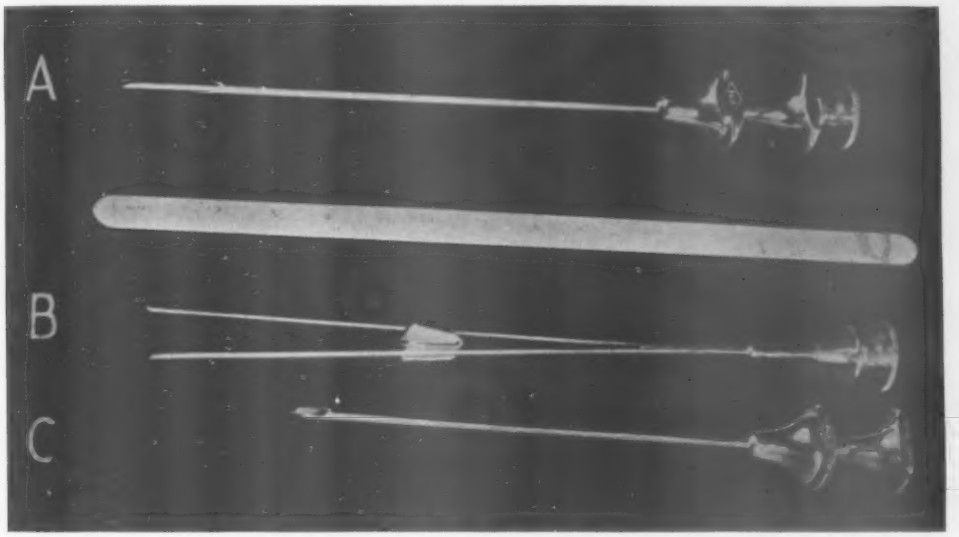

Fig. 10. Silverman biopsy needle. A biopsy specimen is excised by the cutting edges of the pronged cannual *B* when *B* and *C* are assembled as shown at *A*. *C* is the outer sleeve of the assembly *A*, which compresses the excised biopsy specimen between the prongs of *B* when *C* is slid into the tumor to the end of *B*.

conditions in the lymph nodes, he must supply the pathologist with a block dissection specimen.

There are times when the histopathological nature of the tumor in the metastasis may present difficulties in diagnosis even though a suitable biopsy specimen is available for study. Squamous carcinoma of the differentiated grades is easily recognized, but, if a primary carcinoma has not been found, the pathologist may hesitate to classify very anaplastic tumor of the nodes as squamous carcinoma. Of course, the treatment of such an anaplastic tumor mass would be the same whatever the true nature of the neoplasm, but the failure to differentiate a Grade 4 squamous carcinoma from a sarcoma or other radiosensitive

trary, unequivocal terms. The grading of squamous carcinoma is a procedure which requires experience and judgment—the grade is as good as the pathologist. The diagnosis of the grade of a squamous carcinoma is an expression of personal opinion just as is any other diagnosis. Were it not for the fact that the grade of squamous carcinoma is accepted by some physicians as the criterion of radiosensitivity and used by them as a basis for selecting the type of treatment, cancer grading would remain a part of the pure science of cytology. As a simple method of describing the microscopic picture and of grouping cases of squamous carcinoma for reference, microscopic grading is convenient and should be adopted for this purpose by all

pathologists, but as a criterion of the radiosensitivity and prognosis of the squamous carcinoma of the primary growth or of the metastasis, the tumor grade alone is not accurate enough to be of much practical value in the treatment of the individual patient. Some able and experienced cancer therapists believe that there is no way of predicting radiosensitivity. Richards[8] states that cancer has ". . . a variable biological factor which cannot at present be standardized or predicted and probably will never be capable of standardization." Liljencrantz[2] says, "*Only a trial of irradiation* will actually prove a given tumor in a given patient radiosensitive." Clinical experience shows that the theory of radiosensitivity derived from the selective action of low intensity roentgen radiation on the normal cells of the seminiferous tubules of the rabbit has a limited application to the abnormal cells of human squamous carcinoma whether primary or metastatic.

Coutard[1] does not grade squamous carcinoma but uses in another way the information gained by examination of the microscopic slide. He has found the microscopic appearance of value as a practical guide to the intensity and duration of roentgen treatment. He treats the differentiated type of squamous carcinoma of the larynx with smaller doses of roentgen rays administered for a longer time than he does the undifferentiated type.

The failure of tumor grade or any other single aspect of malignancy to predict the outcome of an individual squamous carcinoma is not surprising if one remembers the senility and poor health of many patients having cancer of the mouth and the part which the size and position of the primary cancer plays in the prognosis. Furthermore, one should recall that the statistical method of investigation, which is used to draw conclusions from microscopic and clinical data, is a method which cannot be employed to predict the behavior of an actual individual cancer, but it is valid only for the prediction of the course of a hypothetical average cancer.

Even if one cannot foretell the effect of radiant energy on a particular tumor by studying a microscopic section of the tumor, for other reasons mentioned above, biopsy specimens should be taken from enlarged nodes, squamous carcinoma should be graded, and above all, if irradiation is given, the grade of the cancer in the metastasis should be correlated with the effect produced by the total and the daily number of roentgens absorbed by the metastatic node from the roentgen-ray beam and from implanted radium. A wide adoption of this plan of procedure would assist materially in establishing the value of irradiation in the treatment of metastatic squamous carcinoma of the cervical lymph nodes.

SUMMARY

Unlike the metastases of melanoma of the skin of the face which are multiple, generalized, and unpredictable in location, the metastasis of squamous carcinoma about the mouth appears, with rare exception, as a gradual enlargement of a single cervical node in a location which is predictable and which is determined by the site of the primary cancer; i.e., metastasis always appears first and is often limited to the regional lymph node of the tissue of origin of the primary squamous carcinoma. There are a few cases, of course, with more than one metastatic node and those in which the node has not grown slowly. The primary cancer of these multiple, rapidly growing metastases more often originates in the pharynx than in the mouth, on the lip, or on the face.

Treatment for the prophylaxis of cervical metastasis is unnecessary because metastasis never occurs in a large percentage of cases of squamous carcinoma arising in or about the mouth. The actual percentage of occurrence of metastasis is approximately 25 in cancer of the lip, 50 in cancer of the mouth, and 75 in cancer of the throat.

Contrary to expectation, the clinical diagnosis of small metastases is difficult. In fact, one is as apt to be wrong in diag-

nosis as to be right. Even a large mass cannot be diagnosed by physical examination as a metastasis until the primary cancer is found.

There is good reason to believe that in many cases of cervical metastasis cancer cells are present in the lymph vessels as well as in the lymph nodes. The microscopic examination of multiple sections of block dissection specimens so often shows cancer in tissue which cannot be recognized as nodes that one questions the wisdom of accepting the embolic theory of metastasis as a reliable hypothesis in connection with treatment. One feels, on the contrary, that the field of treatment, irrespective of the method of treatment, must also include lymph vessels about the metastatic node.

In the interest of the science of radiology as well as the welfare of the patient, and of future patients, the clinical diagnosis of cervical metastasis must be confirmed by microscopic examination. To be of scientific value, conclusions regarding the beneficial effect of radiation treatment are possible only when the presence of cancer in the lymph node has been proved by microscopic examination. The patient will not object to the removal of a biopsy specimen from the suspected node if the doctor himself is convinced of the importance of a biopsy specimen.

Small biopsy specimens of suspected nodes may prove adequate for purposes of diagnosis, but block dissection provides the only kind of specimen, from a patient, which gives one an opportunity to study the complete histopathological picture of the involvement of the lymphatic structures of the neck by cancer cells in cases of cervical metastasis.

One must not underestimate the value of the physical examination of the neck in the diagnosis and prognosis of metastasis. If carefully and thoughtfully done, physical examination yields a surprising amount of pertinent information.

It is doubtful if critical analysis of the results of radiation treatment of metastatic nodes (or of the primary cancer) will support the theory that radiosensitivity increases as the grade of squamous carcinoma. Since all metastases are treated to the same extent, namely to the limit of tissue tolerance, proof of the theory of radiosensitivity requires in actual practice that more metastatic nodes containing Grade 4 squamous carcinoma disappear than nodes containing Grade 1 squamous carcinoma. Is this agreement of radiosensitivity and cancer grade in accordance with the reader's personal experience?

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MONO-OSTEITIC PAGET'S DISEASE AS A CLINICAL ENTITY

ROENTGENOLOGIC OBSERVATIONS IN NINE CASES

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OUT of a chaos of chronic deforming osteodystrophies, osteomalacias, and osteosarcomas, Sir James Paget selected a certain type of osteitis deformans to clarify this vast group of deforming bone diseases. His classical description was the first step toward a better understanding of the disease which now bears his name. Paget dealt only with the generalized deforming osteitis, even though there were occasional case reports of singular bone lesions of the same type, which appeared not to fall into his group of osteitis deformans.

A typical example quoted by contraverts of mono-osteitic Paget's disease is a case report by Benno Schmidt, in 1874, of a pharmacist, aged fifty-six, with a saber-shin deformity which was thought at first to be a bone sarcoma and which extended to the opposite tibia and femur three years later.

In 1883 Bowlby reported a case of a cab driver with osteitis deformans of the tibia and progressive bowing for over thirty years. There was no extension of the process to other bones of the skeleton. The patient died from an injury to his head.

After the roentgen ray began to be employed, the problem became more complicated. Indistinct single bone lesions could be seen in the spine where biopsies were impossible. Discussions of such cases filled the literature. The affected vertebrae appeared denser on the roentgenogram, and therefore such terms as "vertebrae noire" or "ivory vertebrae" were used, even though they expressed no disease entity but only an anatomic-pathologic description. Although Schmorl reported a biopsied case of a single bone lesion in a tibia as early as 1905, other mono-osteitic cases were still labelled "hereditary lues," "parakanzer," "localized osteomalacia," and "osteomalacia chronica deformans hypertrophica."

I would like to quote Hallermann for his complete and concise definition of osteitis deformans:

> Paget's disease is a specific, mild disease, without known etiology, which involves one or more bones and parts of bones, characterized by a constant structural change, bone resorption, and regeneration within the bone involved, leading to a secondary medullary fibrosis.

In 1931, Schmorl published all his available data on this subject. He gave a detailed pathologic picture, especially in the gross specimen. His descriptive term "mosaic structure" has done much to differentiate this disease from other similar bone diseases. Schmorl accepted the mono-osteitic form of Paget's disease as an entity, as did Hurwitz and Carr in 1913, but he did not agree that it is a rare finding as stated by these authors. Schmorl, in his observations of 4,603 spines, found the single lesion more frequently than the polyosteitic form. He also stated its most frequent site to be the spinal column. Our observations have been in accordance with his findings, even to the extent of demonstrating two distinct types of Paget's disease in a vertebral body. We found the single bone lesion much more frequently than the polyosteitic form. (Five of our 9 mono-osteitic cases have been seen in this office during three years, and in the same interval only 2 polyosteitic cases were observed.) In 6 of our cases the spine was the most frequent site of involvement (66 per cent).

REPORT OF CASES

CASE 1. T. M., male, aged fifty-five, was first

seen on December 18, 1931, with a history of a fall in June, 1931, and pain on shoulder abduction of five days' duration. Previous roentgen and physical examinations were negative. Although light treatments and aspirin gave no relief, his symptoms subsided under diathermy. There were no complaints referable to his legs.

He returned in July, 1933, complaining of calluses on his feet. At that time he had marked bilateral hallux valgus and relaxed arches, and note was made of a thickening of the left tibia. On August 14, 1933, he returned for a check-up before operation for correction of the hallux valgus and relaxed arches. Full length films of the left tibia and fibula showed a disrupted coarse, dense trabeculation of the medulla, thickening of the cortex, and anterior bowing of the shaft. The other tibia was normal. Skull, spine, pelvis, chest and extremities were roentgenographed and no areas of involvement found. This patient had never complained of his leg, and the deformity was an incidental finding. He dated the bowing back sixteen years and attributed it to constant trauma at the rolling mill in which he was employed (Fig. 1).

The urine and blood pictures were normal. The blood Wassermann reaction was negative. The blood calcium was 12.4 mg. per 100 cc., blood phosphorus 3.9 mg. per 100 cc., and serum phosphatase 8.8 units (Roberts).

He was seen again in October, 1934, having no complaints referable to the left leg. Roentgen examination of the skull, pelvis, spine and extremities was again negative. The lesion in the left tibia showed no change. The transverse radiant lines in the anterior cortex, representing so-called "umbau" zones of Looser, were found to be the same in number as on previous examination.

Fig. 1. Case 1. Anteroposterior and lateral views of the left tibia and fibula showing the typical structural changes of osteitis deformans in the tibia. Note "umbau" zones in the anterior cortex.

Case II. J. S., male, aged forty-four, was first seen on December 1, 1930, complaining of nasal polypi, which were removed. On November 23, 1931, he returned complaining of low back pain of two days' duration. After a roentgen examination which revealed a localized pathologic process in the second lumbar vertebra (Fig. 2 and 3), he was admitted to the hospital.

There was no history of trauma. The pain had appeared suddenly and was severe enough to keep him awake at night. It was spasmodic in character, at just about the level of the iliac crests. It was associated with every spinal motion, was always localized, and did not radiate. When motionless there was no pain. The patient had no other complaints. In 1918 he had pneumonia and an unexplained edema of both legs, without fever, pain, phlebitis, or cardiac symptoms. A left varicocele was removed twenty-six years previously. He had fractured his right tibia in 1923 and his right wrist in 1929. The family history was negative.

Palpation of the spine revealed slight prominence of the second lumbar vertebra with tenderness on pressure. There was muscle spasm, hyperesthesia, and pain associated with every spine motion. The left sacrospinalis muscle group was larger and more prominent than the right. Neurologic and other physical examination was negative; laboratory findings were normal.

Roentgen examination showed an increased density of the second lumbar vertebra involving all of its processes. The body projected anteriorly and posteriorly beyond the normal spinal curvature. Its outline was not as sharp as its neighbors, and trabeculations were widely spaced and coarser than normal. The cortex was thicker than normal, encroaching on the medullary portion of the body. Other bones and skull showed no abnormal roentgen findings.

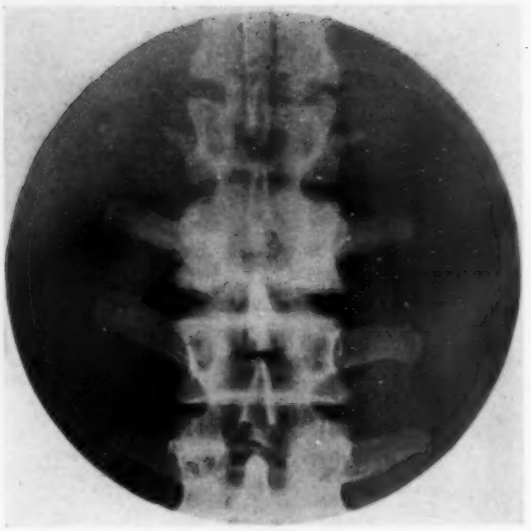

FIG. 2. Case 11. Anteroposterior view of the lumbar spine localized over the second lumbar body. Thia centrum is enlarged in all diameters, showing o decisive increase in density, especially confined te the inferior and superior articulating plates. Thers is some rarefaction in the body of the centrum. Trabeculations are coarse, running roughly parallel in a vertical direction. Lamina and processes are involved by the same process.

The patient refused to wear a brace. He signed a release and left the hospital before any specific treatment could be advised.

FIG. 3. Case 11. Lateral view of the same case as in Figure 2, emphasizing the cortical thickening.

He returned on September 17, 1931, and again on November 25, 1933, presenting the same roentgen findings as before (Fig. 4). The skin over the second lumbar vertebra was reddened, but there was no definite tenderness. There was still spasm and hyperesthesia with motion. The neurologic examination at this time showed decreased sensation to touch and temperature over areas supplied by the first, second, and third lumbar vertebral segments, with increased spontaneous pain over these areas. There was no motor involvement. The reflexes were physiologic. The white blood count was 12,300, with a normal differential count.

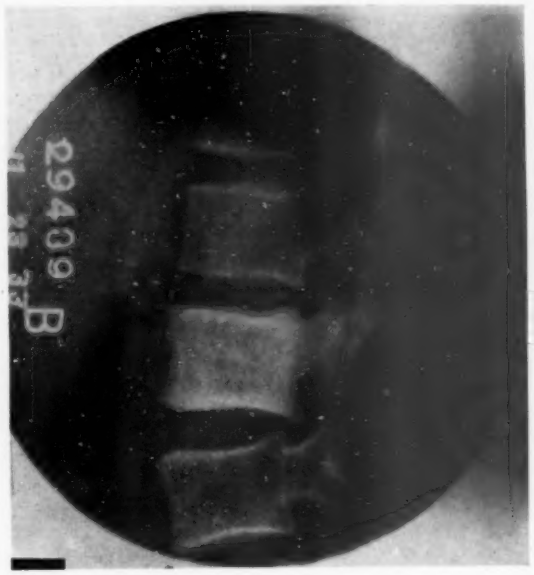

FIG. 4. Case 11. Lateral view of the second lumbar vertebra in 1933 showing no change in its appearance over a period of two years.

Hemoglobin was 100 per cent. The smear was normal. The Wassermann and Kline reactions were 1 plus. Serum calcium was 9.5 mg. per 100 cc., serum phosphorus 3.9 mg. per 100 cc., and serum phosphatase 4.7 Roberts units.

The man was unable to work. He had become irritable and stated that his pain was the cause of this condition. He returned to the roentgen department on February 4, 1935. The second lumbar vertebra showed no roentgenographic change since the first examination in 1931. The skull, pelvis, other vertebrae, spine, and both tibiae were again normal.

On February 2, 1938, the patient was examined elsewhere for a low back pain, and

roentgenograms were taken of the lower spine. These came to my attention, and I recognized the patient's name and the appearance of the second lumbar body. There was no change since the earliest examination seven years before (Fig. 5 and 6).

Case III. B. T., male, aged fifty-five, was seen in November, 1927. He complained of extreme backache over the lower lumbar region of eleven months' duration, loss of appetite, a tired feeling, and incontinence of urine. The family history was negative. His past history revealed an uncomplicated typhoid fever in early life.

Fig. 5. Case II. A check-up view in 1938, showing no change in the appearance of the second lumbar body.

Fig. 6. Case II. Lateral view check-up in 1938. No change of structure since 1931.

Fig. 7. Case III. Anteroposterior view of lower half of the spine including the sacrum showing the dense irregular, enlarged fourth lumbar body. Its trabeculations cannot be made out. The density is of an even character in comparison to the blotchy type of increased density seen in metastatic carcinoma.

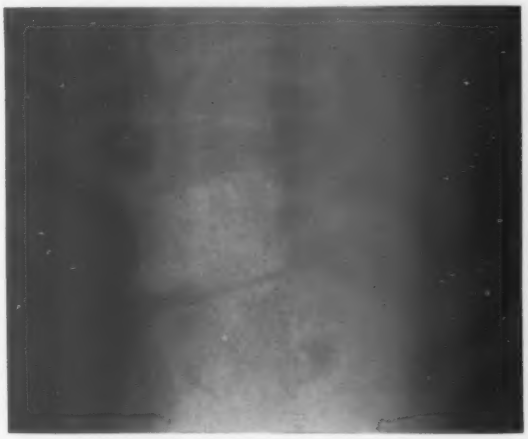

Fig. 8. Case III. Lateral view.

Physical examination revealed a well developed, well nourished male, not acutely ill, with a flaccid paraplegia of the lower limbs. He presented the picture of cardiac decompensation, although little could be elicited by chest

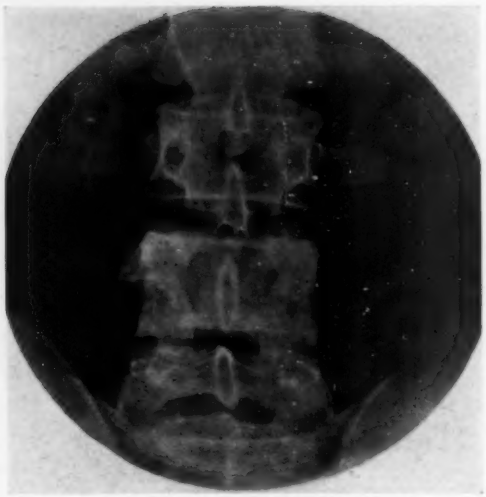

Fig. 9. Case iv. Anteroposterior view of the mid-lumbar section showing the same typical findings in the fourth lumbar as in the previous case. The cortical calcification and thickening are not as pronounced as in the other cases.

Fig. 10. Case iv. Lateral view of the fourth lumbar vertebra in the same case as in Figure 9.

examination. There was edema of the lower limbs, penis and scrotum. The prostate was enlarged. There were no palpable glandular enlargements. His temperature was normal.

Albumin was present in the urine. Roentgenograms of the lumbar spine showed a dense, irregularly outlined, nodular change in the fourth lumbar vertebra. The body projected forward and laterally beyond the normal spinal curvature and was so dense that no trabeculations were visible. The intervertebral spaces were well maintained. The lamina showed definite involvement by the same sclerosing process (Fig. 7 and 8). The patient returned about two months later for roentgen examination of the entire skeletal system. Skull, pelvis, other vertebrae and the long bones showed no abnormality. The lesion in the fourth lumbar vertebra appeared the same as previously. The patient's illness became rapidly worse, and he died shortly afterward. An autopsy was not obtained.

Case iv. A. L., male, aged fifty-seven, complained of "indigestion" and upper right quadrant pain, coming in severe attacks beginning in July, 1936. His past history was irrelevant. There were no other systemic disturbances. The physical examination revealed nothing significant.

A cholecystogram showed stones and a poorly functioning gallbladder, and revealed that the fourth lumbar vertebra was considerably increased in density in comparison with the neighboring bodies. Trabeculation was pronounced, mainly cortical, and the trabeculae appeared to be parallel. The cortex of the body was denser than usual. The lateral diameter was increased, and the body projected slightly beyond the normal anterior and posterior curvatures of the lumbar spine.

The blood Wassermann reaction was negative, blood calcium was 11.1 mg. per 100 cc., blood phosphorus 3.0 mg. per 100 cc., and the serum phosphatase was 12.15 Roberts units. The blood smear was normal. The patient specifically denied any vague back pain or discomfort. A checkup of the entire skeletal system on January 21, 1938, showed no other bone involvement, and the appearance of the fourth lumbar body had not changed at all. The blood calcium was elevated to 12.4 mg. per 100 cc. and the blood phosphorus was 3.65 mg. per 100 cc. at the time of the last visit (Fig. 9 and 10).

Case v. J. C., male, aged fifty-two, had a fall on July 23, 1936. Roentgenograms were taken elsewhere and the eleventh and twelfth ribs found to be fractured. On these films it was noted that the third lumbar vertebra was considerably larger and denser than its neighboring bodies. The trabeculations were coarse and seemed to run in parallel vertical lines. The in-

creased density was mainly due to a dense cortical thickening. It was referred to as "ivory-like" in density. Possible diagnoses suggested were metastatic malignancy from a prostatic carcinoma, Paget's disease, hemangioma of the vertebra. No other bones were roentgenographed to check for multiple lesions.

The patient's family physician found no abnormality or change from the normal on thorough physical examination. The patient worked every day and was watched over a year and a half, showing no indications of metastases. The case was brought to my attention, and I repeated the roentgen examination of the lumbar spine. I was unable to show any change in the appearance of the lumbar body as compared with the first films. The entire skeletal system was roentgenographed and found to be negative. The patient was well in all respects and did not complain of any pain. When questioned about his back he attributed a low backache to his work. He had lost no weight over a period of years (Fig. 11 and 12).

Fig. 11. Case v. Anteroposterior view of the lumbar spine showing the typical structural changes of osteitis deformans in the third lumbar vertebra as seen in previous cases.

Fig. 12. Case v. Lateral view of the lumbar spine.

Fig. 13. Case vi. Collapsed fourth lumbar with resulting scoliosis and rotation of spine. The collapse is all central. Note the recognizable Paget structure in remaining portion of body which has not collapsed. Note sixth lumbar bodies.

The blood Wassermann reaction was negative, blood calcium was 9.2 mg. per 100 cc., blood phosphorus was 3.65 mg. per 100 cc. The serum phosphatase was higher in this case than in any of the previous ones and reached a level of 14.6 Roberts units.

Case vi. Y. L., female, aged fifty-one, was seen in November, 1935, complaining of a low backache with pain radiating into the lower limbs and tingling of the toes, exaggerated on exertion. The backache was of twenty-five years' duration.

When she had first noted this backache a diagnosis of "floating kidney" was made. In

FIG. 14. Case VI. Lateral view.

FIG. 15. Case VI. Anteroposterior view of same patient obtained from New York Clinic taken in 1926. In comparison the collapse is not as marked, and the resultant shifting of the upper lumbar spine as severe as at present. Paget changes are more obvious then because the body has not completely collapsed.

1926, her first roentgen examination (Fig. 15) suggested an "old injury to the fourth lumbar body." Other diagnoses at varying later dates were "hemangioma," "giant cell tumor," and in 1935 "old epiphysitis" and another "diseased vertebrae."

Films taken on these dates showed practically no change in the appearance of the fourth lumbar body. Roentgenograms of the entire skeleton were negative. The last films of the lower spine showed the same disease process as in the previous examination, i.e., a sclerosing cortical lesion with rarefaction and structural changes typical of Paget's disease. The body was collapsing due to softening, resulting in a lateral shifting of the spine. Nerve root compression was probably responsible for the present complaints (Fig. 13 and 14).

Physical examination revealed only marked lordosis and right lateral scoliosis of the lumbar spine with localized tenderness over the lower lumbar segments. The reflexes were normal. The blood calcium was 12.74 mg. per 100 cc., blood phosphorus was 4 mg. per 100 cc., serum phosphatase was 13.3 Roberts units. Smears and routine blood studies were normal, and the Kline reaction negative.

CASE VII. M. M., female, aged sixty-three, complained of a limp and pain in the left hip. This limp started about twelve years previously with occasional pain in the left hip, later on becoming more steady but no more severe. About three to four months prior to admission there was a "definite change for the worse." The pain became more intense, and the limp was more pronounced. There was progressive shortening of the left leg. The history was otherwise irrelevant.

There was no loss of weight or appetite. Physical examination showed distortion of the pelvis with tilting to the right and apparent shortening of the left lower limb, with a compensating lumbar scoliosis. Roentgen examination of the entire skeleton showed normal bone structure throughout except in the left pelvis, defined sharply by the left sacroiliac joint posteriorly and the symphysis pubis anteriorly. The left innominate bone showed typical coarse changes about the acetabulum, obliterating all detailed structure. The entire bone was larger than the right. It bulged medially in the midsection about the acetabulum, suggesting a softening of the bone and compensating new bone formation.

The routine blood examination was negative, as was the Kline reaction. The blood calcium was 12.53 mg. per 100 cc., blood phosphorus 3.816 mg. per 100 cc., serum phosphatase 13.1 Roberts units (Fig. 16 and 17).

Case viii. W. N., male, aged fifty-one, was seen in March, 1939, with the complaint of sharp pain in the low back of one week's duration, following a fall on his back. There were no other complaints. He had complained of low backache for over ten years and had undergone several physical examinations during these years. The diagnosis was "hysteria," and later, on repeated examinations "sciatica," "subacute infection of the lumbosacral joints," "arthritis," and still later, in 1935, "an early destructive lesion, osteitis of the third lumbar body." Physical examination at this time revealed only rather generalized tenderness over the lumbar spine with some lumbar spasm (Fig. 20).

Roentgen examination of the entire skeleton showed normal bone structure throughout except for the third lumbar body which showed a slight increase in size as compared with the neighboring bodies. There was a rarefaction of the internal structure with coarse parallel trabeculations and typical mosaic structure. There was practically no cortical change as contrasted to the other cases of Paget's disease. Comparison of recent films with others taken elsewhere presented no change in appearance in the third lumbar body since 1931 (Fig. 18 and 19).

The first lumbar body was the site of a recent compression fracture. The patient was admitted to the hospital for a spica cast. Blood examination was negative, the Kline reaction was negative. The blood calcium was 11.8 mg. per 100 cc., blood phosphorus 2.1 mg. per 100 cc., serum phosphatase 14.1 units (Roberts).

Another examination in November, 1939, showed no demonstrable change of the third lumbar body. The compressed vertebrae healed normally.

Case ix. A. S., male, aged thirty-five, complained of persistent dull pain in the right hip following a fall. A few days after the injury a diagnosis was made of sarcoma of the right ilium on the basis of roentgen examination elsewhere (Fig. 21).

The left pelvis was normal. The right pelvis was decidedly increased in density throughout, this change being most marked about the acetabulum. There was typical mosaic pattern,

Fig. 16. Case vii. Obvious Paget type bone changes in the left innominate bone, confined to this bone sharply at sacroiliac joint and symphysis. Note bulging of acetabulum medially due to softening of bone.

and trabeculation as seen in Paget's disease. There was no medial bulging of the right pelvis, but the right acetabulum lay at a slightly higher

Fig. 17. Case vii. Overexposed close-up view, localized, of same pelvis as in Figure 16, to bring out structural changes.

Fig. 18. Case VIII. Earliest Paget change in third lumbar body but typical especially in the lower lateral quadrants with resultant bulging (compare with previous cases). Rearrangement of trabeculae and dense stippling. Note mosaic structure, which is better demonstrable now before cortex becomes too dense. This is a typical fibrous type of Paget's disease.

Fig. 19. Case VIII. Lateral view of same case as in Figure 18. There is very little change since 1933, if compared with Figure 20.

Fig. 20. Case VIII. A lateral view taken in 1933 in Chicago of same case as Figure 19. The lacework of trabeculae is not as obvious then, but the changes in the arches and posterior articulating processes are shown better.

level and was deeper partly because of marked cortical proliferation about the acetabular ridge.

Physical examination was negative. Subsequent films taken of the entire skeleton showed

Fig. 21. Case IX. Typical Paget changes observed in the right innominate bone, confined sharply by the sacroiliac joint and the symphysis. The bone is larger, coarser, and denser, with proliferative changes about the acetabulum. Note that there is as yet no medial bulging of the acetabulum, as seen in Case VII.

no other bone involvement. The spine, skull and long bones were negative. The Kline reaction was negative. Routine blood counts and smear were negative. The blood calcium and phosphorus were reported as "normal"; serum phosphatase was 13.6 mg. per 100 cc.

DISCUSSION OF MONO-OSTEITIC PAGET'S DISEASE

As to the etiology of Paget's disease there are still divided ideas. I am inclined to agree with investigators who believe this disease to be a slow infectious process within a bone. There are numerous cases which present a clinical picture of infection: local redness, swelling, and increased surface body heat over the bone affected. There is pain and tenderness. There is periosteal reaction to a possible low grade infection. Malignant changes are seen occasionally. If we can establish a definite entity of a mono-osteitic form of Paget's disease we must look for our etiologic factor locally and not generally as was previously thought. There is no concrete proof that the parathyroids are the cause of the trouble. Calcium and phosphorus levels are normal in Paget's disease.

The lesion must be infectious in nature and may be arrested in its progress as soon as the entire bone is involved. During the early active infection, metastatic foci may be set up in other bones.

The usual arterial calcification present in all cases of Paget's disease seems to be a contributary factor rather than primary. The decreased local blood supply may interfere with a local immunity in a bone against a low grade infection.

Today we accept osteitis deformans as a disease entity, separate from osteitis fibrosa cystica, though ten years ago such men as Assmann thought there was a common etiologic factor for both diseases and that each was a different manifestation of the same disease. Hallermann distinguished between these two diseases in 1929. Schmorl also proved two distinct entities in his reports.

The next problem concerns the delimitations of the disease. Is mono-osteitic Paget's disease a distinct entity or should it be considered an early manifestation of the generalized disease? No discussions have appeared in the English literature since Schmorl published his work. The lapse of discussion since 1931 may be construed as an acceptance of mono-osteitic Paget's disease as a definite entity.

We agree with the earliest authors that when they described doubtful bone lesions and deformities of long bones, no one could state with certainty the extent of the disease in the entire skeleton. Their conclusions were uncertain. There is no doubt that the disease is mainly a roentgenological problem, and because of that fact, our conceptions have become more definite and conclusive. Today the roentgen ray offers a method for study not only of the nature of the disease but also of the extent of the lesion. Is it mono-osteitic or poly-osteitic? We have had cases under observation long enough to be convinced that Paget's disease can occur in one bone only and never become generalized.

As Newton stated fifteen years ago, the lesion is entirely a roentgenological problem in its non-clinical form and no biopsy is necessary. In 1933, Jaffe wrote:

> A critical analysis of the reported clinical cases of the monostatic group shows, however, that only a small number properly belong to this group, for included among reported cases are instances of other local bone diseases, which have been improperly classified, especially localized forms of fibrocystic disease, lues, and forms of bone tumors.

The disease is so definite and regular in the change it produces in the bones involved that to the experienced eye it is recognizable and can be differentiated from the changes in the bones seen in osteitis fibrosa cystica, angioma, osteomalacia, osteomyelitis, lues, and osteoplastic metastatic new growth.

Improved roentgenologic technique in demonstrating bone detail is responsible for our being able to recognize two different types of bone changes in mono-osteitic Paget's disease of the spine.

Schmorl has described the two different Paget types in his voluminous work on pathology of the spine. He has found that part of a vertebral body may be involved early in the disease, but that soon the entire body, with its processes and often its spurs, if any are present, will be uniformly involved. It has also been observed that the lesion extends into the neighboring body through hypertrophic spurs if they form a complete bridge across the intervertebral space.

TABLE I

SUMMARY OF CASES

	Case	Sex	Age	Part Involved	Duration of Symptoms	Type of Complaint	Serum Phosphatase Level*
I	T. M.	M	55	Left tibia	None	Bowing of leg	8.8 mg.
II	J. S.	M	44	Second lumbar	Two days	Short stabs of pain localized in low back	4.7
III	B. T.	M	55	Fourth lumbar	Ten months	Localized backache	Not done
IV	A. L.	M	57	Fourth lumbar	None	None (accidental finding)	12.15
V	J. C.	M	52	Third lumbar	None	None (accidental finding)	14.6
VI	Y. L.	F	51	Fourth lumbar	Twenty-five years	Early: low backache; late: sharp radiating pain legs	13.3
VII	M. M.	F	63	Left innominatum	Twelve years	Little pain in hip, mainly limping	13.1
VIII	W. N.	M	51	Third lumbar	Ten days	Low backache	14.1
IX	A. S.	M	35	Right innominatum	Six days	Dull hip pain following fall six days previously	13.6

* Morrell-Roberts units

It has been said that the term "osteitis deformans" does not apply to the disease in the spinal column. We find affected vertebral bodies to be definitely deformed. The body involved by Paget's disease is enlarged and its trabeculae are coarse, dense, and interlacing, giving us the familiar mosaic structure (the term first employed by Schmorl). There is also a change in shape: a narrowing of the sagittal diameter or thickness.

The disease is characterized by a constant "umbau" (tearing down and building up) of new bone. Trabeculae are fewer, coarser, thicker, and surprisingly softer. The cortical tissue becomes heavier, thicker and denser in structure, probably with some periosteal bone deposit. Long bones in the lower extremities bow because they are softened and weight bearing. The innominate bone is definitely denser, enlarged, and bows inward and upward. The acetabulum becomes deeper and rides higher, resulting in a limp. In the vertebrae one type shows a dense cortical frame which has developed because of a fusion of the thick outer layer of trabeculae. The trabeculae in the center of the body become fewer in number, forming a coarse lacework. This type of Paget's disease eventually collapses under the pressure; the degree of collapse varies. In some cases there is only a decreased sagittal thickness and an enlargement of the body in other diameters. In one of our cases there was at first slight and later complete collapse with a resultant slipping of the body above.

In the other type of Paget's disease, there is more generalized involvement of the vertebral body. The entire body is extremely dense throughout. Its trabecular structure is thickened and coarse; there is no specific dense frame around a hollow body. The segment is enlarged uniformly in all dimensions. The appearance is that of an "ivory vertebra," and there is a problem in differentiating it from similar forms as seen in marble bones, osteoscle-

rotic anemias, leukemia, malignant lymphogranuloma, myeloma (infrequently osteoplastic), osteoplastic metastatic lesions from carcinoma of prostate or breast, and lues. This vertebra withstands a weight bearing pressure and does not collapse.

The non-collapsing type of osteitis deformans is usually without pain or other symptoms, whereas the collapsing type is definitely painful, probably because of compression of the body so minute that it is sometimes not demonstrable roentgenographically. Later symptoms are referable to the further mechanical effects resulting from nerve root compression.

The cases presented show blood chemistry changes similar to those observed by Gutman and Kasabach. The serum calcium and serum phosphorus are within normal levels. The important change is in the serum phosphase activity which is elevated in all polyosteitic cases whereas there may be no or only slight elevation in mono-osteitic cases. The highest value reached in our series of cases was 14.6 units (Morrell and Roberts), which is considerably less than the 59.5 to 130.3 units (Bodansky method), reached in the advanced polyosteitic cases reported by Gutman and Kasabach. There is therefore a direct relationship between the measurable serum phosphatase activity and the extent of bone involvement in the skeleton.

Usually the single bone lesions are found accidentally during roentgen examinations for irrelevant abdominal complaints or during examinations after injury. If the lesion is not located in the spinal column, where it may be symptomless, deformities of the pelvis or long bones give the chief complaints. Spinal lesions are usually spoken of as "non-clinical" because of the absence of clinical findings. Two of our cases gave severe symptoms of nerve root compression localized over the involved spinal area, whereas 3 cases gave no symptoms referable to the findings in the spine.

The lesion is never "generalized," but polyosteitic or mono-osteitic from the onset, and develops rather rapidly in any bone once it shows any sign of involvement. I have observed a femur in a polyosteitic form of Paget's disease which presented such an extreme involvement and bowing over a period of a year and a half that the leg was one and a half inches shorter than in the previous examination, when it showed only some cortical thickening below the lesser trochanter. This contradicts our former concept of Paget's disease as a slowly progressive lesion. Once the whole bone is involved, the lesion reaches an arrested stage and remains so for any number of years. There may be years of slow progressive bone changes due to compression, or even sarcomatous change may develop.

Generally speaking, one can say that Paget's disease does not occur below the age of forty years, but one of the cases presented here is that of a patient only thirty-five years old. Schmorl encountered no instance before the age of forty in 4,603 routine spinal dissections which undoubtedly held many symptomless cases. There must be many cases of mono-osteitic disease in a non-clinical form which do not come under observation until later ages, during examination for some irrelevant trouble.

SUMMARY

1. Nine cases of localized Paget's disease (mono-osteitic) have been presented; the histories, follow-up examinations, and long observation seem to prove that mono-osteitic Paget's disease does not become polyosteitic.

2. Paget's disease is either polyosteitic or mono-osteitic.

3. Mono-osteitic Paget's disease is a distinct entity, not an early stage of a polyosteitic disease, and, though often unrecognized, a more common form than the polyosteitic type.

4. The mono-osteitic form may be of two basic types: (a) a fibrotic, rarefying structural change with softening of bone resulting in deformities, or (b) a sclerotic osteoplastic new bone formation mainly of cortical or periosteal source.

5. Once the disease develops it progresses

rapidly until the affected bone is completely involved and then there is no further recognizable progress.

6. The lesion is most often seen in the lumbar bodies and is essentially a roentgenologic problem in diagnosis, since this is the only means of recognizing it.

7. The blood phosphatase activity is indicative of the amount of bone involvement.*

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* Since the evidence of this paper has been compiled, 3 more cases of mono-osteitic Paget's disease have come to my attention.

Two of these cases, both of which were localized to the right tibia, were in a mother and her son. The mother was over sixty years of age and the son was forty-two. The mother had complained for over twenty-five years of a painless bowing of the right lower leg which had become painful the last half year. The son complained of no pain, but had noticed a similar bowing in his right lower leg during the past five years. The rest of the skeleton was negative in each patient. These cases are of interest because of the apparent familial nature of the disease in this instance. It should be of interest to investigate this phase of osteitis deformans further.

The third case is a biopsied one. It is the only case which was subjected to a biopsy, and therefore was proved by pathologic section.

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ROENTGENOLOGIC DIAGNOSIS OF LEFT-SIDED APPENDICITIS

REPORT OF A CASE

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IT IS believed that a diagnosis of left-sided appendicitis, made entirely by roentgenologic means, and confirmed by surgical operation and pathological examination, is sufficiently rare and of enough interest to warrant reporting. A small number of reports of left-sided appendicitis have been found in the literature, but all of them seem to have been diagnosed clinically in patients who were found to have situs inversus viscerum, or by surgical operation and finding the appendix on the left side. The case herein reported showed an incomplete rotation of the colon which was not discovered until the roentgenologic examination was made. All of the other viscera were normally located. The pain of which the patient complained was located in the left side of the abdomen just above the level of the anterior iliac spine. There was no pain or tenderness in the right lower quadrant. Clinical examinations by a competent internist and a competent surgeon had led both to suspect a diverticulitis, and the patient was referred for roentgenologic examination of the colon with a presumptive diagnosis of "diverticulitis."

EMBRYOLOGY

According to Bailey and Miller[1] and Lee[4], the cecum is in the left iliac fossa alongside the descending colon up to the third month of intra-uterine life. At this time, the ileum enters the cecum from the right. At the end of the third month of intra-uterine life, the cecum rotates and ascends to reach the right iliac fossa somewhat similar to the unfolding of a fan, the mesenteric attachment representing the handle. When complete rotation has occurred, the right portion of the colon crosses the duodenum in the upper portion of the abdomen and the ileum enters the cecum from left to right. Failure of rotation, or stoppage at any point, may determine the position of the appendix. In transposition of the viscera the appendix would naturally be found on the left because of the "mirror-image" relationship to the normal.

CLASSIFICATION

Hembrow[3] classifies left-sided appendices as falling into one of four different groups: (*a*) complete or incomplete transposition of the viscera; (*b*) non-rotation of the colon (*c*) imperfect fixation of the cecum and ascending colon; (*d*) excessively long appendix with the tip to the left of the mid-sagittal line.

In discussing appendicitis, Hembrow believes that pain should be felt in the right lower quadrant of the abdomen in cases of: (*a*) non-rotation of the colon; (*b*) imperfect fixation of the cecum, and (*c*) excessively long appendix with the tip to the left of the midline of the body. He feels, however, that pain should be felt in the left lower quadrant in cases of complete transposition of the viscera. Block and Michael[2] believe that pain should be localized in the right lower quadrant, no matter what the cause of location of the left-sided appendicitis, and Pol[7] says that the pain may be located on either side. Nix and Nix[6] are of the opinion that repeated attacks of appendicitis, resulting in adherence of the appendix to the left side of the abdominal wall, should cause the clinical symptoms to be manifested on the left.

INCIDENCE

LeWald,[5] in 1925, in a study of the incidence of left-sided appendices, found 1 case of complete transposition of the viscera in

5,000 necropsies, 29 cases of complete transposition of the viscera in 40,000 roentgenologic examinations, and 9 cases of non-rotation of the colon in 40,000 roentgenologic examinations.

Nix and Nix[6] have recently reported an incidence of 0.071 per cent left-sided appendicitis in a series of 4,215 appendectomies and state that "left sided appendicitis, according to Walther, occurs once in every one thousand cases." Of the 3 cases reported by these two writers, 2 were due to incomplete transposition of the viscera, while the remaining 1 was attributed to imperfect fixation of the cecum and ascending colon. Reports in the literature would indicate that left-sided appendicitis is found more frequently in cases of transposition of the viscera.

CASE REPORT

J. M. M., a white male, aged forty-five, was referred to me for roentgenologic examination of the colon on May 5, 1942. The presumptive diagnosis was "diverticulitis." His complaint, on the day of examination, was of pain in the lower left quadrant of the abdomen, nausea, and a slight amount of fever. This had persisted for about two weeks. The patient gave a history of having had similar attacks of pain in the left side of the abdomen over a period of eight or ten years, usually accompanied by low-grade fever, always accompanied by nausea, and sometimes accompanied by vomiting. Various opinions had been offered by different physicians he had consulted in the past, but none had suspected an appendicitis. A number of different types of medication had been prescribed for these attacks, but the patient had determined for himself that bed rest and an ice cap to the abdomen had been most effective.

Fig. 1. Non-rotation of the colon with appendix on the left.

Fig. 2. Lateral roentgenogram showing the position of the appendix, cecum, and portions of the colon.

Preliminary palpation of the abdomen at the beginning of the roentgenoscopic examination revealed no rigidity or distention of the abdomen, though the patient showed a definite tenderness on the left side which was most pronounced just above the level of the left superior iliac spine. The routine roentgenoscopic examination of the chest showed no gross evidence of abnormalities or disease of the intrathoracic viscera. There was no impediment to the entry of the barium mixture into the colon. When the barium suspension reached the mid-portion of the transverse colon, it was directed downward and sharply back toward the left so that the proximal half of the transverse colon and a portion of the ascending colon were parallel to the distal half of the transverse colon, and the cecum lay parallel to the descending colon and anterior to it. No masses or evidences of adhe-

Fig. 3. Air contrast roentgenogram showing filling defect at the tip of the appendix.

sions were found in the abdomen so the unusual position of the proximal half of the large bowel was attributed to a congenital non-rotation. The cecum and the first portion of the ascending colon were spastic and were definitely tender to pressure. The appendix showed an excellent filling with the barium mixture and palpation here elicited an increasing degree of tenderness as the tip was approached. The tip of the appendix was painful to pressure and was accompanied by an increase in the patient's nausea.

Roentgenographic examination of the colon consisted of a roentgenogram made with the colon filled with as much of the barium suspension as the patient would tolerate (Fig. 1), a roentgenogram made after the colon was emptied as well as possible, a roentgenogram made in the lateral position (Fig. 2), and an air contrast roentgenogram (Fig. 3). These roentgenograms showed the position of the appendix in the abdomen. There was a moderate sized filling defect at the tip of the appendix (Fig. 4) which was interpreted as probably being a fecalith. The roentgenologic diagnosis of "left-sided appendicitis, subacute to chronic, probably with a fecalith at the tip" was made.

Six days later the appendix was removed through a left rectus incision. A large inflammatory mass, containing pus in its center, was present at the tip of the appendix and was adherent to the mesentery of the small bowel in the left side of the abdomen. It was not adherent to the left wall of the abdomen at any place. The report of the surgeon's findings was: "The first 2 inches of the appendix pointed mesially toward the right, then made an acute turn caudally. The tip of the appendix, which contained a moderate sized fecalith, was found involved in an inflammatory process which ultimately was discovered to be an abscess containing 2 or 3 ounces of creamy, foul-smelling, pus." The inflammatory mass involved the mesentery of the small bowel of the left side, though the surgeon did not identify the mesentery further. Sulfanilamide powder was sprinkled in the abdomen about the site where the mass was removed and the abdomen was closed with a cigarette drain. The patient made an uneventful recovery and was discharged on the twelfth postoperative day.

The pathologist reported macroscopic findings of "subacute and chronic appendicitis imbedded in a mass of inflammatory and fatty tissue," and a microscopic diagnosis of "acute peri-appendicitis with acute local peritonitis."

DISCUSSION

While it is not within the scope of this paper to enter into a discussion of the nature and localization of reflex pain in

Fig. 4. Enlarged view of the appendix showing the filling defect at the tip.

visceral disease, it is felt that none of the theories mentioned in the first part of this paper are fully applicable in explaining the symptomatology of this particular case.

The pain was located on the left side at the time of the physical and roentgenologic examinations, and the patient was emphatic in stating that it had never been felt to the right of the mid-sagittal line. This is neither in agreement with the belief of Block and Michael[2] that the pain of left-sided appendicitis of all types should be felt in the right lower quadrant, nor with the statement of Hembrow[3] that appendicitis in cases of non-rotation of the colon should give right-sided symptoms.

The location of the pain on the left side is also difficult to explain embryologically. It would seem reasonable to assume that the nervous system of the embryo would be sufficiently developed for determination of the visceral nerve tracts by the time the cecum would rotate to its normal location in the right lower quadrant. Failure of rotation should have no effect on the viscerosomatic nerve reflexes, and the pain should be felt in the right lower quadrant.

There was no evidence, after the abdomen was opened, of adhesions between the appendix and the left abdominal wall, so that the explanation advanced by Nix and Nix[6] did not apply in this case.

Pol[7] felt that pain might be located on either side. One of the 2 patients reported by him had right-sided pain and was proved to have a complete transposition of the viscera. In the other patient the tip of the appendix was adherent to the cecum, and this one suffered from left-sided pain.

I am of the opinion that the location of the pain on the left side in the case herein reported was a result of involvement of the mesentery of the small intestine of the left side in the inflammatory mass which arose from from the tip of the appendix. It seems reasonable to assume that painful impulses originating from the relatively large area of mesenteric involvement might have been sufficient in number and intensity to subordinate painful impulses arising from the appendix and, in that way, account for the patient's complaint of pain in the left side of the abdomen.

The explanations offered by other writers for the right-sided location of pain in left-sided appendicitis seem to be reasonable and correct in the absence of certain complications. It also appears to be reasonable to expect left-sided pain in left-sided appendicitis in case of adhesions to the left abdominal wall. Pol's second case, together with the case herein reported, led me to believe that left-sided pain may also be caused by adherence and involvement of the mesentery of the left side of the abdomen in an inflammatory process originating from the appendix.

SUMMARY

1. A diagnosis of left-sided appendicitis made by means of roentgenologic examination alone is reported.

2. A possible explanation of left-sided pain in left-sided appendicitis is added to those opinions previously expressed by other writers.

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ROENTGENOGRAPHY OF SOFT TISSUES BY MONOCHROMATIC ROENTGEN RADIATION AND COLOR-FORMING DEVELOPERS

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A ROENTGENOGRAM is a record, upon a silver halide emulsion, of shadows of varying density produced by the passage of roentgen rays of different wave lengths through objects of specific chemical composition and structure.

The recording of these shadows is dependent upon two main factors: (*a*) electrotechnical factors; (*b*) darkroom processing.

The electrotechnical factors can be subdivided into two groups: (*1*) constant; (*2*) variable.

The constant and variable groups comprise all of the different conditions that are necessary in order to secure a roentgenogram of proper detail, contrast and density with a minimum of distortion. The constant group includes the regular routine of a roentgenologic laboratory regardless of its size and specialization: exact calibration of the output of the roentgen-ray transformer, stability of current, exactness of the timing devices, freedom from jerking of the Potter-Bucky diaphragm, positioning of the subject, alignment of the roentgen tube, etc.

The variable group includes those factors which can be changed at will in order to produce roentgenograms of different characteristics. These main factors are: time, distance, kilovoltage and milliamperage.

While errors in the manipulation of the different devices will result in roentgenograms of poor detail, contrast or density, which can be traced to improper distance, kilovoltage, milliampere-seconds, defects in accessories, etc., the fogging of the film by "secondary radiation fog" is one factor which has received inadequate consideration. It is, perhaps, this radiation fog factor above all others, considering the standard and accepted methods of procedure, which is chiefly responsible for the lack of satisfactory differentiation of shadows produced by objects of slightly differing opacities upon the silver halide emulsion. This separation of shadows, greatly increased by special darkroom procedure, makes possible the roentgenography of soft tissues without sacrificing the detail of bony structures.

From the time of the discovery of x-rays by Roentgen in December, 1895, great progress has been made. The powerful transformers now in use, the rectification of the wave by valves, the advent of the rotating anode roentgen tube permitting heavier loads on very small focal spots, the increase in speed and latitude of the roentgen films, the elimination of some of the secondary radiation by grids, the use of intensifying screens of various speeds are all factors which when properly combined produce the modern roentgenogram quite rich in information.

Of great importance is the incident radiation from the anode of the roentgen tube. The beam of radiation that is produced at this point is a heterogeneous beam composed of roentgen rays of different wave lengths and consequently of different penetrating powers. This power of penetration of a certain radiation is a function of its hardness or wave length, the shorter the wave, the greater the penetrating power of the radiation. The formation, however, of roentgen radiation at the anticathode following the impact of rapidly moving electrons is a rather complex phenomenon, to which a completely satisfactory answer has not as yet been given. It is known that two kinds of radiation are produced at the anticathode of a roentgen tube when

voltage is applied to the terminals of the tube. According to Barkla, and other experimenters, whenever a swiftly moving electron is stopped at the anticathode, an electromagnetic impulse is emitted out into space. Its field is contained between two spheres that are described about the place at which the retardation or stoppage is effected, and which widen out with the speed of light (Sommerfeld). The distance between the two spherical shells gives the measure of the width of the zone of disturbance, i.e., the "width of the impulse." Since the discovery of Laue, it has been referred to, in the language of spectra, as the wave length of the particular radiation and the sum of all of the impulse radiations as the continuous spectrum of the radiation. At the same time through the action of the cathode rays the atoms of the material of the anticathode are thrown out of their position of rest and tend to return to the same. In so doing they emit frequencies natural to, or characteristic of, the material of which the anticathode is composed, these frequencies being always of the same wave length regardless of the kilovoltage used within definite limits. This radiation is the characteristic radiation which depends entirely upon the atomic weight of the emissive material of the anticathode. In the language of the spectra this is the line spectrum of the radiation. This characteristic radiation is always constant, while in the impulse radiation the hardness of the ray depends on the voltage used, which means that the region of wave lengths of greater intensity in the continuous spectrum shifts towards the smaller wave lengths as the voltage increases.

The beam of roentgen rays produced by an ordinary roentgen tube is obviously heterogeneous and contains many wave lengths. To the continuous spectrum must be added, above certain voltages, the characteristic radiation; thus the penetrating power of the radiation emitted at a known kilovoltage is greatly supplemented by radiations of longer wave lengths.

As the kilovoltage applied to the terminals of the roentgen tube increases, the wave length of the radiation decreases. At a given kilovoltage there is a radiation of a certain penetrating power. This particular radiation at this kilovoltage is predominant. Advantage of this fact is taken in roentgenography of the human body where the penetration of the radiation is determined by increase or decrease of the kilovoltage in proportion to the thickness and structure of the part roentgenographed. At the same time other radiations of different wave lengths are produced; those with a shorter wave length than the predominant are not intense, while those with a longer wave length remain abundant. These latter because of their low penetrating power have no desirable rôle whatsoever in the making of the roentgenogram. According to Clark, "A mixture of rays consisting of three parts, soft, hard, and very hard constituents, with equal density, when filtered through five millimeters of aluminum, the very hard ray penetrates 80 per cent, the hard ray 60 per cent and the soft only 4 per cent. Thus, out of a continuous heterogeneous mixture actually generated, a beam less and less heterogeneous and with greater and greater average hardness (shorter wave length) results from greater filtration." This point is clearly demonstrated in the density curves plotted from different thicknesses of aluminum filters in which the use of a 5.5 mm. filter of aluminum makes the curve become almost linear indicating no more change in the quality of the radiation. These curves agree with those of Clark and other observers. It does not mean, however, that the radiation obtained after this filtration is absolutely monochromatic. It does mean that all wave lengths that are very long, and therefore have a low penetrating power, have been removed from the incident radiation and only the effective wave lengths of the particular kilovoltage used are allowed to penetrate. The characteristic secondary radiation of aluminum is of no importance as it requires only a few centi-

meters of air to filter it completely.

The incident roentgen radiation, in passing through a scatterer (and the human body may be considered as such) partly goes through without any change, save perhaps attenuation in intensity without any change in wave length, and is partly transformed into radiation of another sort. The portion of the radiation that goes through has been estimated to be 0.1 of the incident beam. The portion that is absorbed is transformed into several types of radiation which collectively form "secondary radiation." Two of the components of this secondary radiation are of interest in roentgenography, namely: scattered roentgen radiation and characteristic secondary roentgen radiation. The first exhibits in its general hardness quite the same properties as the incident primary beam and is thus in character independent of the nature of the secondary radiator. On the other hand, the relative intensity, that is to say, the fraction that is sent out as scattered roentgen radiation depends on the secondary radiator. This radiation goes out from the secondary radiator in all directions in space, but in general the radiation is stronger in the direction of the primary beam. Since the incident radiation is heterogeneous, when no filtration is used, so is the scattered radiation. The characteristic radiation which is emitted from a given secondary radiator is homogeneous and always possesses the same hardness, independent of the hardness of the incident radiation. It is characteristic of the element in question and goes out into space in all directions without any one being favored.

As the primary beam has a photochemical effect upon the silver emulsion of the roentgen film causing silver particles to become darkened after chemical processing in proportion to the intensity of the radiation at any given point, so too the secondary radiation has the same photochemical effect upon the silver emulsion, with the exception that while the effect of the primary radiation is proportional or dependent upon the intensity of the beam, which in turn is a function of the thickness of the scatterer, the effect of the secondary radiation is not proportional to the intensity of the primary beam, but its effect is nearly uniform over the entire film area producing the so-called "secondary radiation fog." This radiation fog spreads uniformly over the entire area of the film obliterating the very faint shadows produced by tissues of low opacity and small thickness and at the same time marring the brilliance and detail of shadows produced by heavier structures. Since the absorption and scattering of radiation of long wave lengths, particularly by heavy elements, accounts for a great deal of the unmodified scattering, elimination of this radiation at the source will *per se* abolish the consequent secondary radiation and secondary radiation fog, thus making possible the visualization of shadows of different density. Upon this point is based the roentgenography of soft tissues by monochromatic roentgen radiation.

If the predominant radiation given out by a known kilovoltage adequately penetrates a subject of a given thickness, the filtration of the incident radiation through aluminum filters, 3 to 7 mm. in thickness (5 mm. of aluminum having been found satisfactory for all types of work—see density curves), while slightly attenuating its intensity without changing the predominant wave length, will eliminate noneffective, roentgenographically, long wave radiations which in turn will produce in their passage through the scatterer copious secondary radiation fog. Elimination of this secondary radiation fog will avoid obliteration of shadows cast by tissues of low density and will also prevent the marring of detail produced by tissues of different density and thickness. A true shadowgraph of long range latitude will be the result. Compensation for the slight attenuation of the intensity of the incident radiation by its filtration can be made by increasing the time of action by 25 per cent

of the original standard technique. Kilovoltage, distance and milliamperage remain the same.

DARKROOM PROCESSING

Examination of a finished roentgenogram, from the purely technical viewpoint, is the only means of determining what, if anything, was done incorrectly during processing. Although lack of detail, contrast, poor density, blurring, can be traced directly to electrotechnical errors, quite often these and other faults are the direct result of faulty technique during the pure processing of the roentgenogram in the darkroom.

It is assumed that the contact of the intensifying screens is perfect, that their speed and age, the size of the focal spot of the roentgen tube, the ratio of the Potter-Bucky diaphragm and all other electrotechnical factors are well known and properly accounted for. The problem then revolves about the film itself and its photographic treatment.

The ideal film is one with a high speed, high contrast, very small grain emulsion and very wide latitude. The speed of the film and the size of the grain are, unfortunately, opposite to each other. So far manufacturers of roentgen films feel that a large grain size is essential for high speed. High contrast and wide latitude, although not exactly opposites, are almost so. A film with a wide latitude is more desirable even at the expense of some high contrast. A rapid transition from black to white prevents the recording of some soft structures. The blackening of the photographic film is the logarithm of the number that expresses how many times a beam of light is reduced in passing through the film. In a film with a long range of blackening the density is almost proportional to the logarithm of the intensity.

The size of the silver grain in the ordinary roentgen film is somewhat enlarged when the film is developed in standard developers. For a number of years experimentation with films and plates of very small grain has been conducted, but these have not been adaptable to roentgenography because of their lack of sufficient speed. Since a film of this quality is not obtainable developers known to diminish considerably the size of the grain have been tried. The length of time, however, required to process the film was a serious handicap. Fortunately, in the process of research attention was called to a developer, claims for which were fine grain photographic images in a color-forming process. This developer, patented by duPont Film Manufacturing Corporation, was not generally available and had never been used for roentgenologic work.

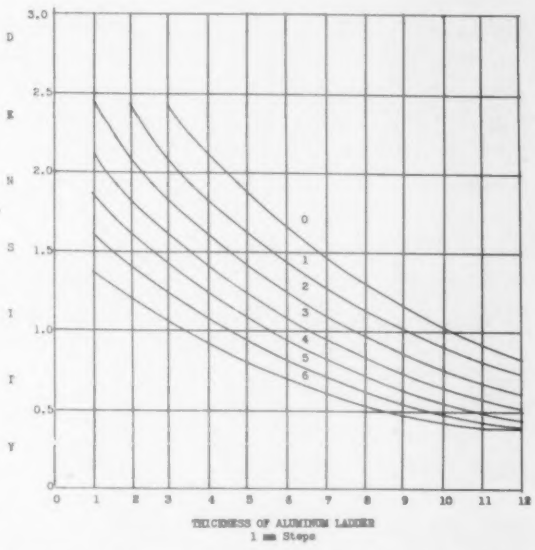

Chart 1. Curves of density versus thickness of aluminum through filters (aluminum) showing the homogenizing effect of filtering the incident heterogeneous beam of roentgen rays emanating from the roentgen tube.

Compare unfiltered curve with those produced by filtration through different thicknesses of aluminum.

$$D = \log_{10} \frac{F_0}{F_1}$$

F_0, luminous flux which falls upon the film area.
F_1, luminous flux which is transmitted through the film.

While basically the formula is practically

FIG. 1. Shows uniform density of entire bony structures of the pelvis as well as the soft tissues.*

the same as described in the patent, some changes were necessary in order to adapt it to this special work. The mixing is rather tedious and demands exactness not only in weighing of materials, but also in the subsequent steps. The developer oxidizes very rapidly, which means it cannot be stored but must be made fresh every time it is used. Because of this, tank development is impossible, and trays must be used. One thousand cubic centimeters of developer will develop six 14 by 17 inch films or their equivalent of other sizes. The fixing of the film is the same, although we prefer to use a fresh chrome-alum-acetic

FIG. 2. Roentgenogram of the pelvis showing almost empty bladder and mass within the pelvis.

* The black and white reproductions do not show clearly the detail and contrast seen in the original blue and white films.

FIG. 3. Lateral view of the pelvis showing soft tissues and skeletal parts.

FIG. 4. Lateral view of the abdomen showing anterior abdominal wall as well as the spine.

Fig. 5. Lateral view of the dorsal region showing uniform density throughout the spine and other skeletal structures.

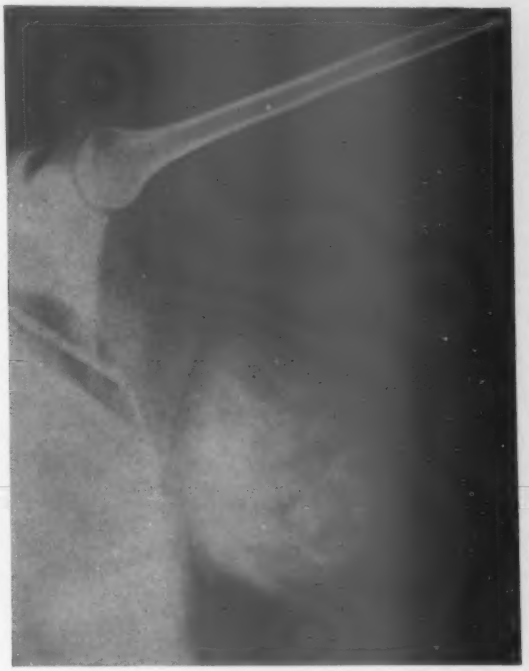

Fig. 7

Fig. 6

Fig. 8

Fig. 6, 7 and 8. Roentgenograms of breast and axilla, showing skeletal parts of the shoulder and ribs as well as the structure of the breast, lymphatic nodes of the axilla, muscles of the arm and subcutaneous tissues.

FIG. 9

FIG. 10

FIG. 11

FIG. 12

FIG. 9, 10, 11 and 12. Roentgenograms of the extremities showing muscular layers, adipose tissue, tendinous attachments and skeletal parts.

Fig. 13. Roentgenogram of the chest showing uniform density in bronchial and vascular structures.

Fig. 16. Roentgenogram of the skull showing uniform density throughout as well as the cervical spine.

Fig. 14

Fig. 15

Fig. 14 and 15. Roentgenograms of the neck showing cervical spine, larynx, trachea and soft parts of face and neck.

acid fixer. The formula for this developer as we use it is as follows.

A.		
1. p-aminodiethylaniline monohydrochloride	1.5	grams
2. p-aminodimethylaniline monohydrochloride	1.5	grams
B.		
3. p-nitrophenylacetonitrile	0.75	gram
4. Phenacyl chloride	0.75	gram
5. Alpha naphthol	0.50	gram
6. Ethyl alcohol, 95 per cent	75.0	cc.
C.		
7. Sodium sulfite anhydrous	5.0	grams
8. Sodium carbonate anhydrous	25.0	grams
Water to make	1000.0	cc. (liter)

Dissolve No. 1 and 2 in a glass flask in 225 cc. of water at room temperature. These two chemicals are very soluble and give a purplish solution. Keep flask away from strong light.

Dissolve No. 3 in No. 6 (ethyl alcohol). Shake vigorously for several minutes. It takes some time before this chemical is completely dissolved; an amber colored solution results. When No. 3 is completely dissolved, add No. 4 and shake also until dissolved. When no particles can be seen floating, add No. 5 and shake well. Keep this material separate and well stoppered in a glass container. Dissolve C (No. 7 and 8) in 700 cc. of water in a separate glass flask.

Mix together A and C. A slightly purplish solution is obtained. Cool this solution to 70° F. and add B to it. A bright red solution is formed which on shaking begins to darken almost immediately. Keep away from light and use within ten minutes in an open tray. When the solution is poured on the tray, it will appear as a reddish-brown liquid. It will have a very strong, pungent odor which will make the eyes water quite freely due to the phenacyl chloride which is a "tear gas forming" chemical. The time required to develop a film in the above solution is from seven to nine minutes at 70°F. Thorough washing before placing the film in the fixer is absolutely necessary.

The above solution will give roentgenograms tinted in blue. The amount of dye that is deposited in the film is proportional to the actinic activation of the silver at any point. Thus, the developer is very selective, and its range is quite considerable from an almost pure white, where no radiation has passed through the emulsion, to a very dark blue, in the freely exposed parts of the film. It produces a roentgenogram with a very fine grain silver dye image which increases materially the detail of the film. The contrast is medium and, when used with films of wide range latitude, the separation of shadows of very low density is very apparent. It should be stated that rapid pace in the darkroom is essential for the production of fine grain roentgenograms. Films should be dried within an hour.

Modifications of the above developer can be made whenever certain conditions are to be emphasized. For example: if greater contrast is desired as might be the case in strictly bone work, the amount of alpha naphthol could be increased to 0.75 gram. This chemical being such a powerful reducing agent will, in larger quantity, increase the density of the shadows, perhaps by forcing a larger deposit of the dye on the emulsion. Likewise, the color can be changed to a reddish blue or purple by using No. 1 exclusively and using 3.0 grams instead of 1.5 grams. The methylation of a dye brings its color more towards the blue and ultraviolet; thus, by using No. 2 exclusively a rather flat grayish-blue will be the color of the roentgenogram. The combination of No. 1 and 2 has been found to be excellent.

Should films have a markedly reddish color, or be entirely light red, it means that the developer has oxidized. In developing a set of films, all of them (six 14 by 17 inch in 1,000 cc. of solution) should be developed at the same time. That is, one should be placed in the tray right after another, taking care that the solution has covered completely the first and each subsequent film. Air bubbles and sticking of the films to each other should be avoided; after the films are all in the tray, rocking of the tray helps prevent these conditions. Constant changing of their relative places is also helpful. This is done by taking the film at the bottom of the tray and placing

it on the top of all of them. This procedure must be repeated for each film. In addition to insuring proper coverage by the developer of the entire surface of the film on both sides, it presents the opportunity to observe the progress made.

Developing hangers should be at hand so that when the film is thoroughly developed, it can be clipped to the frame, then washed, fixed, washed again and dried in the standard manner. It should be mentioned that although during the process of examination of the films while developing, visualization of the soft tissues is practically lost after a few minutes, the film will clear considerably when finished, and these structures will reappear distinctly.

Roentgenograms processed in the solution described above keep as well as roentgenograms treated by accepted methods of darkroom procedure.

IONIZATION OSCILLOGRAMS*

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ALTHOUGH every radiologist is familiar with the textbook descriptions of wave forms such as half wave, full wave, constant potential, etc., very few have ever seen them demonstrated because the apparatus needed for such a demonstration is so elaborate that it is found only in a few well equipped physics laboratories. Again it must be remembered that this wave form is that of the electrical energy and that the wave form of the roentgen-ray emission may not necessarily be identical.

The process described here is a relatively simple one which permits immediate observation as well as photography of the time/intensity pattern of the actual roentgen-ray emission. It uses a thimble ionization chamber whose output is amplified and fed into a cathode-ray oscilloscope. The ionization chamber and oscilloscope are of the conventional types but the successful coupling of them depends on a single step, high gain amplifier recently developed by one of the authors.[1]

The complete set up is shown in Figure 1, the ionization chamber being placed in the roentgen-ray beam at such a distance from the tube that it receives about 80 r per minute, the wave appearing on the screen of the oscilloscope where it may be observed at length or photographed.

As the amplifier was described in a physics journal not commonly read by radiologists, a brief description may be in order. It was designed as a measuring instrument for clinical dosage, and though not stable enough over long periods of time to be used as an absolute standard, it proved to be an excellent instrument for such work as phantom measurements because after calibration it shows the roentgen output on the meter with practically no time lag. Fluctuations in the roentgen-ray beam are seen on the meter as no timing factor is involved. The complete instrument is shown in Figure 2. The vacuum tube and grid resistor are contained in the metal box attached to the ionization chamber and the box is filled with melted paraffin. A three-conductor shielded microphone cable of any convenient length connects it to the small steel cabinet which contains the batteries, switches and meter. The circuit is shown in Figure 3. Attention is called to the fact that this instrument has sufficient gain in the single tube to take the ionization current from a thimble chamber and reproduce it on a 0–1 milliampere meter. Though the ordinary 1T4 radio tube is used in this circuit it is absolutely essential that it be selected and prepared for this use. To prepare this tube it is set upon the bench without ionization chamber, shielding, or buck circuit but with all batteries as shown in complete diagram and with a 0–10 ma. meter in plate circuit. When first turned on, the tube will draw about 4 ma.; however, at the end of three hours some tubes will drop to about 1.4 ma., others remaining constant over the entire time. Only those tubes that show the current drop are suitable for this use, though all tubes may test exactly the same before and after on the commercial checker. About six out of ten tubes tested will prove suitable. In the completed instrument, the plate current will start high when first turned on, stabilizing itself in a few minutes,

[1] Taft, R. B. A vacuum tube x-ray intensity meter. *Rev. Scient. Instruments*, May, 1942, p. 234.

* Presented at the Forty-third Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 15–18, 1942.

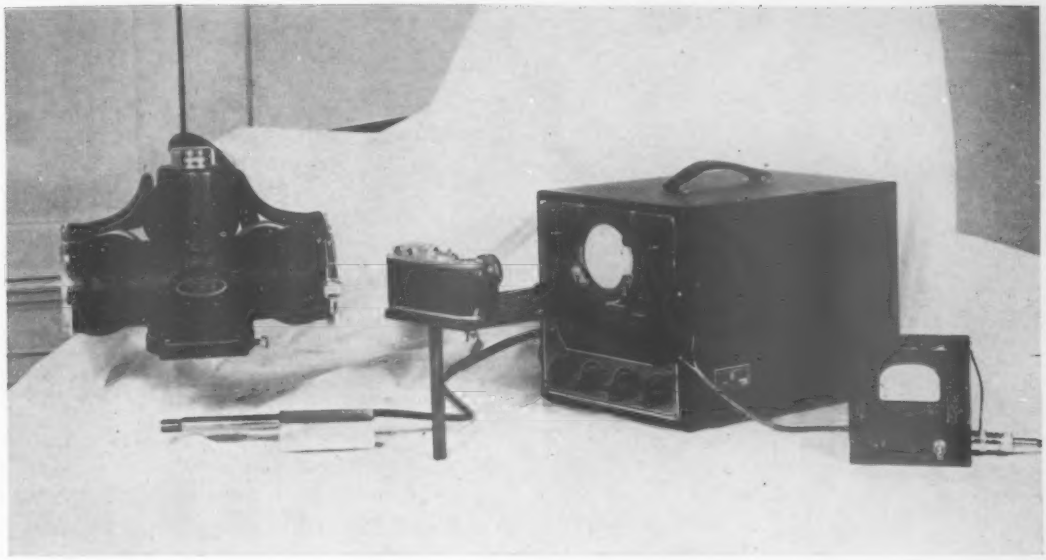

Fig. 1. Apparatus. In actual use, ionization chamber is placed in beam and 20 foot cable allows meter and oscilloscope to be placed in another room where operator is protected.

after which the meter is set to zero by adjusting the resistance in the buck circuit and it is ready for operation.

The amplifier is coupled to the oscilloscope by placing the primary of a 2:1 ratio audio transformer between the positive lead of the "B" battery and ground, the secondary being connected to the imput leads of the oscilloscope.

Any oscillosope is suitable for this use but it is strongly recommended that one of fairly high sensitivity (0.26 volts RMS per

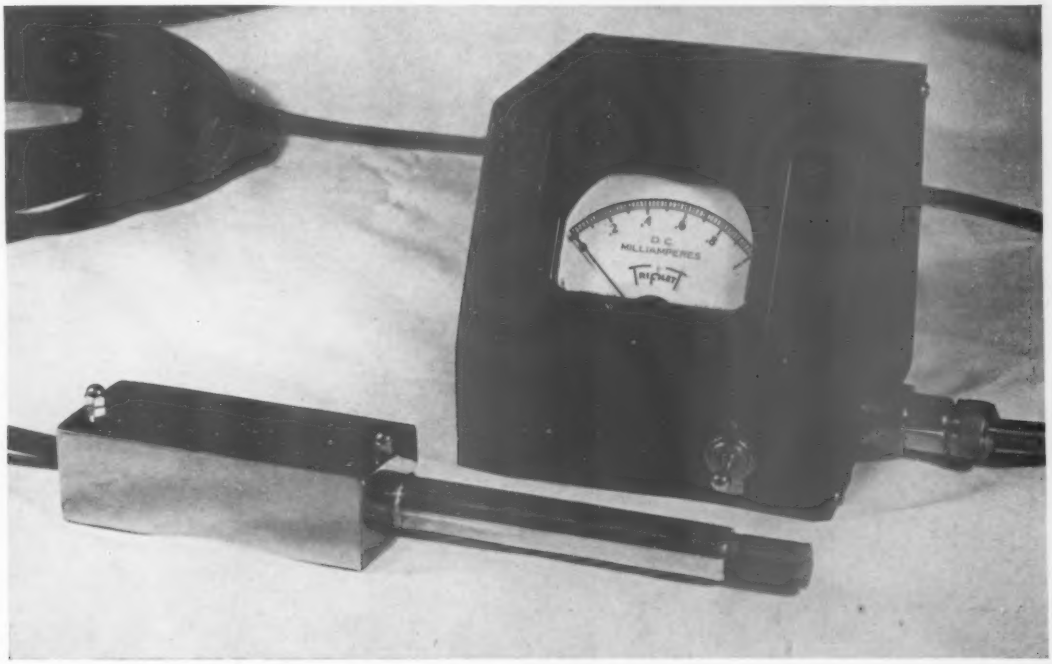

Fig. 2. Vacuum tube intensity meter.

inch on screen) be selected as otherwise sufficient amplitude will not be obtained to fill the screen with the pattern without producing distortion.

When photographs of the screen are desired a good miniature camera with an f 2 lens and extension collar is suggested. If much of this work is to be done, a stand which fastens the camera to the oscilloscope at the exact distance and position, such as is shown in Figure 1, is a great help. As most commercial films have little green sensitivity, an exposure of about 1/10 second at f 2 is needed but with such a film as the Agfa Fluororapid the exposure may be reduced to 1/100 second. In certain cases where it is desirable to record fluctuating patterns on motion picture film, the old style safety film will be well exposed at f 2, sixteen frames per second.

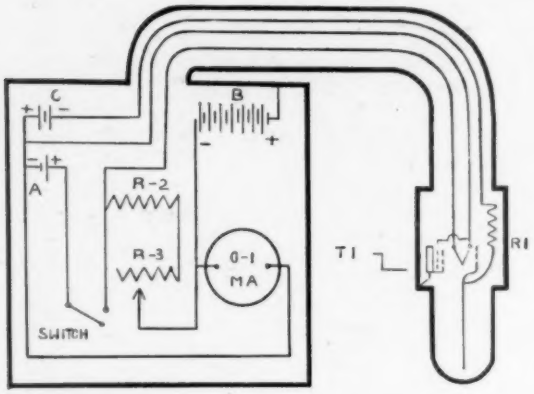

Fig. 3. Diagram of intensity meter. *T1*, Type 1T4 radio tube; *A*, 1½ volt battery; *B*, 67½ volt battery; *C*, 4½ volt battery; *R1*, 1,000 megohms, *R2*, 500 ohms; *R3*, 1,000 ohms.

Patterns from several conventional roentgen-ray machines are shown in Figure 4. Obviously all parts of the apparatus must be properly grounded and all electrical connections properly made or freak patterns may result. An example of such a pattern is shown in Figure 4*D* where a test was being made on an old disk rectified

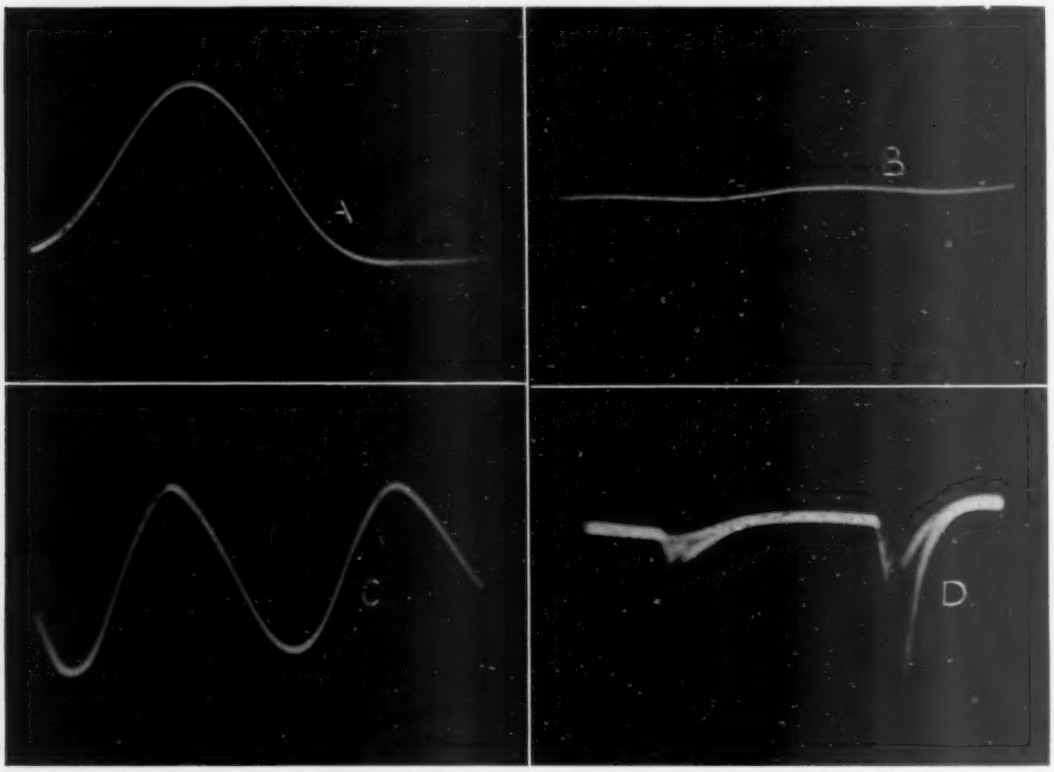

Fig. 4. Oscillograms. *A*, Villard; *B*, constant potential; *C*, four valve; *D*, false pattern, not from ionization but failure to ground apparatus.

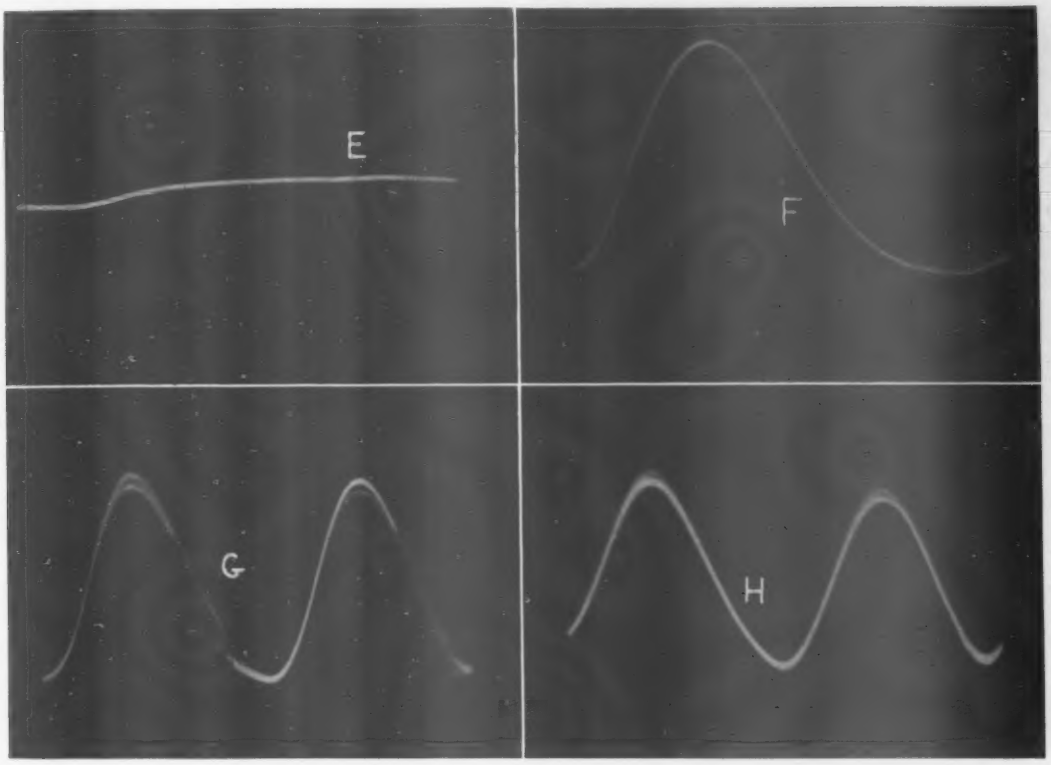

Fig. 5. Oscillograms. *E*, half wave, 80 foot cables at 3 ma.; *F*, same as *E* but at 30 ma.; *G*, old cross arm mechanical rectifier; *H*, same as *G* but with RF chokes in aerial leads.

machine connected to a shock proof tube but with the cables apparently not properly grounded. Placing the ionization chamber near either of the cables and totally out of the roentgen-ray beam gave the same pattern. The difficulty could not be eliminated until an aluminum ionization chamber was substituted for the lucite one, the lucite with its graphite inside coating having insufficient conductivity to prevent an inductive effect on the collector electrode.

One interesting feature is shown in Figure 5. A half-wave rectification machine was used in connection with shock-proof cables totalling about 80 feet. Here it is shown in Figure 5*E* that a 3 ma. emission is not that of half-wave rectification but of constant potential; however, the same setup when operated at 30 ma. (Fig. 5*F*) gave the characteristic half-wave pattern. This demonstrates that the procedure is capable of determining whether the capacity of the system is sufficient to give constant potential at all loads expected of it.

Figure 5*G*, and *H*, shows the improvement in the pattern obtained from an old cross arm mechanical machine when RF chokes were placed in the leads to the tube.

One of the most interesting patterns was accidentally found to be given off from a rotating anode tube (Fig. 6). This same full-wave generator gives a perfectly normal pattern from an ordinary tube but the rotating anode tube gave a fluctuating pattern which on a still photograph could not be properly shown. The fluctuation appeared separately in each alternation and was greatest when the anode was gaining speed. The fluctuations "looked exactly the way the rotor sounded." The tube was giving perfect roentgenographic service and a pinhole roentgenogram showed normal focal spots, both small and large. Despite the fact that we had just started this experimental work and were none too

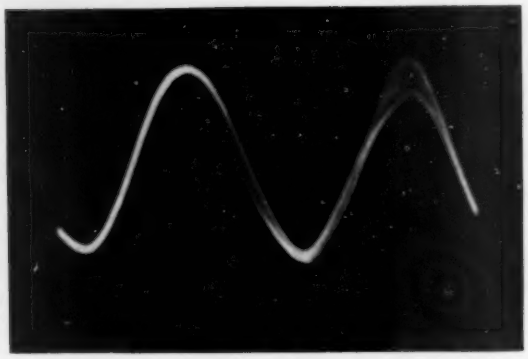

Fig. 6. Rotating anode tube, four valve, defective anode.

sure of the apparatus, we felt that there was something the matter with this tube. This idea was substantiated when the next four rotating anode tubes tested all gave perfectly steady patterns. The explanation which seemed most logical was that there was a place on the anode which gave less radiation as it passed the focal spot and as the speed of the anode is almost but not quite synchronous, a beat note was being formed. When this tube was finally replaced after completion of service, the manufacturers kindly gave us a photograph of the anode (Fig. 7) which shows plainly the cause of the curious pattern.

In conclusion, it is believed that the ionization oscillogram is more than a spectacular demonstration of wave forms and has proved useful in the determination and correction of faults in roentgenologic equipment.

Fig. 7. Photograph of anode showing peeling of tungsten.

ADDENDUM

After this paper had gone to press, the question was raised by several physicists as to whether the time factor of the amplifier was great enough to cause some distortion of the wave forms. It was shown that with a grid leak of 1,000 megohms and a capacity of about 30 mmf, the time constant would be relatively long compared to 1/120 second.

While it is conceded that this time factor would not interfere with the purposes for which the instrument is used in this paper, it is probable that other uses may arise where it would be undesirable, In order to eliminate any argument, one can greatly reduce the time constant simply by using a large ionization chamber and a low resistance grid leak.

Recently a chamber has been constructed of thin masonite approximately 4×4×2 inches in size. This is coated with aquedag and has a single collector electrode of aluminum wire. No metal is used in the chamber except one aluminum rivet to establish contact. When this chamber is placed close to the roentgen tube so that it receives about 400 r per minute, sufficient ionization current is obtained to give a full scale oscillogram with a grid leak as low as 5 megohms.

The potential for the chamber is about 420 volts and is obtained by bringing a well insulated lead directly from the DC voltage supply in the oscilloscope. Any slight ripple is eliminated by placing a ½ mf condenser by the chamber and a 2 megohm resistor in the line.

The low resistance grid leak makes the instrument very stable, so that it is no longer necessary to embed the amplifier tube in paraffin, which still further reduces the capacity of the system.

This appears to remove all possible criticisms of the method.

DISCUSSION

Dr. W. Edward Chamberlain, Philadelphia. Doubtless an electrical engineer would prefer to study "wave form" with conventional methods of voltage and current oscillography. But to the radiologist there is much appeal in a method which measures what comes out of a roentgen tube rather than what goes into it or

is applied to it by way of the high tension generator leads.

Eighteen years ago Newell and I* attempted to make this type of study. While we did not achieve a direct oscillographic tracing such as the excellent ones of Dr. Taft, we did obtain an analysis of the wave form in terms of the roentgen-ray *output* and it is obvious that our aim was identical with that of this present work.

From the above circumstance it is easy to see why I am so enthusiastic about Dr. Taft's oscillograms. That they have practical value as well as theoretical interest is shown by the following anecdote.

When Dr. Taft arrived at Temple University Hospital for the purpose of collaborating with Dr. Henny, we watched him "analyze" the wave form of several of our units with great interest. We were particularly anxious to learn as much as possible about a new, four-valve cable connected generator in which the enclosure of valve tubes, transformer and high tension leads is so complete that only such a method as Dr. Taft's could be used for its study. To our astonishment the ionization oscillograms revealed a half-wave pattern instead of the expected full-wave type of oscillogram. What followed was a real triumph for Dr. Taft and his method because the service men and engineers were very insistent that the apparatus was functioning normally, as a four-valve, full-wave machine. They even got Dr. Taft up on a ladder to look down into the transformer oil tank, to see with his own eyes that all four of the valve filaments were lighted. Dr. Taft stuck by his guns, of course, since there was no mistaking the significance of the half-wave oscillographic tracing, and when the transformer tank was actually opened it was found that two of the four valve tubes had never been connected to the circuit. As soon as the proper connections were installed, the expected full-wave oscillographic pattern materialized.

Another very practical application of this simple device is for the measurement of the "ripple" in the output of a therapy unit, or the "ripple" in the fluoroscopic beam where low milliamperage and extra long cables tend to produce a "constant potential" wave form in a unit that was designed for full-wave rectified, pulsating operation.

Dr. George C. Henny, Philadelphia. The electrical circuit used in the ionization chamber amplifier is grounded to the shield case and to the ionization chamber. The collector electrode is therefore approximately at the negative potential of the "B" battery which is about 67.5 volts. The question may well be asked "How do you know that you have reached the saturation potential of the ionization chamber?" Careful measurements were made to check this point. By observing the output meter while applying decreasing voltages to the ionization chamber, the latter being in a roentgen-ray beam of constant intensity (135 r per minute) it was found that at 65 volts there was still 98 per cent saturation. This is sufficient for practical purposes in making oscillograms, particularly at this fairly high roentgen-ray intensity.

It might be of interest to you to know that the current amplification of the 1T4 tube as used in this circuit is 184,000. If the intensity of the roentgen-ray beam to be studied is a little below the range of the apparatus, the ionization current can be increased by substituting another ionization chamber of the same size which is lined with gold leaf. When this was done the ionization current for a certain roentgen-ray beam was increased 12.6 times. In doing this, however, the ionization chamber no longer approaches the air-wall equivalent condition. This implies that the ionization within the chamber depends a great deal upon the quality of the roentgen-ray beam being studied

* Chamberlain, W. E., and Newell, R. R. Wave form and efficiency: analysis of roentgen therapy machines. Am. J. Roentgenol. & Rad. Therapy, 1924, *12*, 509–513.

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Twenty-eighth Annual Meeting: 1943, cancelled.

EDITORIAL

AN EVALUATION OF ANGIOCARDIOGRAPHY

SINCE Robb and Steinberg[1] introduced their method of visualization of the chambers of the heart, the pulmonary circulation and the great blood vessels in man, a great deal of interest has been shown in the subject and several reports have appeared in the literature from time to time, but the method has not come into general use. However, those who have continued its use remain enthusiastic about the possibilities of this examination. The method has been applied sufficiently by certain observers so that they are able to draw some conclusions not only concerning its use but the value which may be derived from this method of study in depicting the normal anatomy of the heart and the great vessels in vivo.

Quite recently Taylor and McGovern[2] have summarized the examination of one hundred persons by the Robb-Steinberg method and have drawn certain conclusions from these cases, particularly regarding the normal anatomy of the heart and great vessels. Their examinations have shown variations from the recognized and accepted roentgenographic anatomy of the cardiac silhouette in the normal as well as in the abnormal. From an analysis of their material, they indicate that existing concepts concerning the size, shape and position of the heart chambers and the thickness of its muscles are at variance with those observed in the adynamic viscus in the cadaver, and that certain concepts require modification in the light of observations made in vivo.

In contrast to the accepted concept concerning the anatomic positions of the cardiac chambers and the great vessels they point out certain variances, namely that there is a deep location of the ventricular conus, that the pulmonary aorta as it arises from the ventricle is situated deep in the cardiac silhouette and does not form a prominence on the left border of the heart. That portion of the cardiac silhouette above the base of the left ventricle and below the left pulmonary artery is usually not opacified with contrast substance and must indicate an area that is not hollow but solid. Their observations further led them to the conclusion that the middle cardiac segment of the left border of the heart is formed by the pulmonary aorta and the left pulmonary artery. The non-opacified portion of the lower right cardiac border seen in angiocardiography is the inferior vena cava and, contrary to the accepted view, the right heart does not occupy the major portion of the cardiac silhouette in the postero-anterior projection in roentgenograms of the chest, but the left ventricle occupies a considerable portion of the cardiac silhouette instead of, as previously supposed, only a small strip along the left cardiac silhouette.

Such fundamental observations as those of Robb and Steinberg, Sussman and his associates,[3,4] and Taylor and McGovern have stimulated a renewed interest in roentgenography of the cardiovascular system, and it is from such careful analyses of a large group of cases that definite progress will be made in roentgenography of the cardiovascular system. In addition, a clearer concept will be gained of the normal anatomy

[1] Robb, G. P., and Steinberg, I. Visualization of the chambers of the heart, the pulmonary circulation, and the great blood vessels in man. Am. J. Roentgenol. & Rad. Therapy, 1939, *41*, 1–17.

[2] Taylor, H. K., and McGovern, Teresa. Evaluation of angiocardiography. *J. Am. M. Ass.*, April 17, 1943, *121*, 1270–1276.

[3] Steinberg, M. F., Grishman, A., and Sussman, M. L. Angiocardiography in congenital heart disease. I. Dextrocardia. Am. J. Roentgenol. & Rad. Therapy, 1942, *48*, 141–146.

[4] Steinberg, M. F., Grishman, A., and Sussman, M. L. Angiocardiography in congenital heart disease. II. Intracardiac shunts. Am. J. Roentgenol. & Rad. Therapy, June, 1943, *49*, 766–776.

of the heart as well as of the pathological processes of the cardiovascular system in the living. As Sosman[5] rightfully points out, contrast cardiography still remains in the realm of a highly specialized procedure and only those thoroughly equipped to carry out the method should attempt it. But it is from such studies that methods come into more general use with the elimination of the technical hazards entailed in such examinations. From these studies, moreover, a vast amount of information may be obtained which can be used in the daily routine studies of the cardiac silhouette.

[5]Sosman, M. C. Discussion of paper by Taylor and McGovern.[2]

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual Meeting: 1943, cancelled.

American College of Radiology
Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill.

Section on Radiology, American Medical Association
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: 1943, cancelled.

Arkansas Radiological Society
Secretary, Dr. J. S. Wilson, Mack Wilson Hospital, Monticello, Ark. Meets every three months and also at time and place of State Medical Association.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Drake Hotel, Chicago, Ill., Nov. 29–Dec. 3, 1943.

Radiological Section, Baltimore Medical Society
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

Section on Radiology, California Medical Association
Secretary, Dr. J. D. Coate, 434 Thirtieth St., Oakland, Calif.

Radiological Section, Connecticut Medical Society
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets bi-monthly on second Thursday, at place selected by Secretary. Annual meeting in May.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

Radiological Section, Los Angeles County Medical Association
Secretary, Dr. Donald R. Laing, 65 North Madison Ave., Pasadena, Calif. Meets on second Wednesday of each month at the County Society Building.

Radiological Section, Southern Medical Association
Secretary, Dr. Roy G. Giles, Temple, Texas.

Brooklyn Roentgen Ray Society
Secretary, Dr. Leo Harrington, 880 Ocean Ave., Brooklyn, N.Y. Meets monthly on fourth Tuesday, October to April.

Buffalo Radiological Society
Secretary, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months.

Chicago Roentgen Society
Secretary, Dr. Warren W. Furey, 6844 S. Oglesby Ave., Chicago, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

Cincinnati Radiological Society
Secretary, Dr. Samuel Brown, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

Cleveland Radiological Society
Secretary, Dr. J. O. Newton, 13921 Terrace Rd., East Cleveland. Meets at 6:30 P.M. at Midday Club on fourth Monday each month, October to April, inclusive.

Denver Radiological Club
Secretary, Dr. Edward J. Meister, 366 Metropolitan Bldg., Denver, Colo. Meets third Friday of each month at Denver Athletic Club.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Building.

Florida Radiological Society
Acting Secretary, Dr. Walter A. Weed, 204 Exchange Bldg., Orlando, Fla. Meetings in May and November.

Georgia Radiological Society
Secretary, Dr. James J. Clark, 478 Peachtree St., Atlanta, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

Radiological Society of Kansas City
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month at a place designated by the president.

Illinois Radiological Society
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. H. C. Ochsner, Methodist Hospital, Indianapolis. Meeting held the second Sunday in May annually.

Kentucky Radiological Society
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

Long Island Radiological Society
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

Louisiana Radiological Society
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

Michigan Association of Roentgenologists
Secretary, Dr. E. M. Shebesta, 1429 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

Milwaukee Roentgen Ray Society
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

Minnesota Radiological Society
Secretary, Dr. Annette T. Stenstrom, 1218 Medical Arts Bldg., Minneapolis, Minn. One meeting a year at time of Minnesota State Medical Association.

Nebraska Radiological Society
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

New England Roentgen Ray Society
Secretary, Dr. Hugh F. Hare, Lahey Clinic, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

Radiological Society of New Jersey
Secretary, Dr. H. J. Perlberg, 921 Bergen Ave., Jersey City. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

New York Roentgen Society
Secretary, Dr. H. H. Kasabach, Presbyterian Hospital, New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

North Carolina Roentgen Ray Society
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

North Dakota Radiological Society
Secretary, Dr. L. A. Nash, St. John's Hospital, Fargo. Meetings held by announcement.

Central New York Roentgen Ray Society
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Ohio Radiological Society
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati. Meets at time and place of annual meeting of Ohio State Medical Association.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport.

Philadelphia Roentgen Ray Society
Secretary, Dr. R. P. Barden, University Hospital, Meetings first Thursday of each month from October to May inclusive at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

Pittsburgh Roentgen Society
Secretary, Dr. R. G. Alley, 4800 Friendship Ave. Meets second Wednesday each month, 4:30 P.M., October to June, Pittsburgh Academy of Medicine.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Sidney Larson, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. A. M. Popma, 220 N. First St., Boise, Idaho.

St. Louis Society of Radiologists
Secretary, Dr. P. C. Schnoebelen, 462 N. Taylor Ave. Meets fourth Wednesday of each month, except June, July, August, and September, at a place designated by the president.

San Francisco Radiological Society
Secretary, Dr. H. A. Hill, 450 Sutter St., San Francisco. Meets monthly on third Thursday at 7:45 P.M., first six months at Toland Hall, second at Lane Hall.

Shreveport Radiological Club
Secretary, Dr. R. W. Cooper, Charity Hospital, Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M., September to May inclusive.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. Herman Klapproth, Sherman, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. E. L. Flanagan, 116 E. Franklin St., Richmond, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Thomas Carlile, 1115 Terry St., Seattle. Meets fourth Monday each month, October throughMay, College Club, Seattle.

X-ray Study Club of San Francisco
Secretary, Dr. J. M. Robinson, University of California Hospital. Meets monthly in evening on third Thursday.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets monthly on third Thursday from November to June inclusive, at 8:15 P.M., 32 Welbeck St., London.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine 1, Wimpole St., London, W. 1.

Faculty of Radiologists
Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1 England.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive.

Canadian Association of Radiologists
Secretary, Dr. A. D. Irvine, 540 Tegler Bldg., Edmonton, Alberta.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

South America

Sociedad Argentina de Radiologia
Secretary, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

Continental Europe

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse Biel. Meets annually in different cities.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad: USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

FIRST INTER-AMERICAN CONGRESS OF RADIOLOGY

In the May, 1943, issue of the JOURNAL appeared an announcement of the meeting of the First Inter-American Congress of Radiology to be held in Buenos Aires, Argentina, from October 17 to 22, 1943. Since that announcement was made the official speakers for the special subjects to be discussed have been chosen. These are as follows:

1. Roentgen Diagnosis of Spinal Infections. Dr. Di Rienzo, Argentina, Dr. Opazo, Chile, and Dr. Caminha, Brazil. Collaborator: Dr. Riera Bauzá, Chile.

2. Cancer of the Breast: Treatment and Results. Dr. Butler, Uruguay, Dr. Guzmán, Chile, Dr. Nelson de Carvalho, Brazil, and Drs. Puente Duany and Fonts Abreu, Cuba.

3. Roentgen Diagnosis of Diseases of the Gastrointestinal Tract. (a) Inflammation of the jejuno-ileum. Dr. Maissa, Argentina. (b) Inflammation of the Colon. Dr. Esguerra Gómez, Colombia, and Dr. J. J. Vallarino, Panama. Collaborators: Dr. Burlando, Argentina, Dr. Caminha, Brazil, and Dr. Elizondo Martel, Cuba.

4. The Teaching of Radiology in the Americas. Dr. Oscar Soto, Perú. Collaborators: Dr. Vignoles and Dr. Varsi, Argentina.

There will be an exhibition of roentgenograms. Those who have already signified their desire to take part in this exhibit are Drs. Martinez Olascoaga, Pisano Blanco and Vazquez Piera, Uruguay, Dr. Quirno Codas Thompson, Paraguay, and Dr. Cassio M. Vilaça, Brazil.

New Faculty Building, Buenos Aires, Argentina, in which the First Inter-American Congress of Radiology will be held.

The Congress is to be held in the beautiful new Faculty Building shown in the accompanying illustration. This photograph shows but part of the large construction project now under way which, when completed, will be known as the Policlínica San Martín.

Correspondence regarding the Congress should be addressed to the Secretaria General del 1er Congreso Inter-americano de Radiologia, Alsina 3117, Buenos Aires, Argentina.

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Head

Grant, F. C., Webster, J. E., and Weinberger, L. M.: Unusual symptomatology with tumors of the cerebellum based on 158 verified cases 271

Epstein, B. S.: Skull laminagraphy 272

Peyton, W. T., and Peterson, H. O.: Congenital deformities in the region of the foramen magnum: basilar impression 272

Neck and chest

Duncan, R. E.: Pulmonary tuberculosis; its exclusion from the Navy 272

de Lorimier, A. A.: Mass roentgenography of the chest for the United States Army ... 273

Pollock, W. C.: Tuberculosis in the Army .. 273

Hodges, F. J.: Fluorographic examination of chest as a routine hospital procedure ... 274

Pindell, M. L.: Photoroentgenography in a tuberculosis program 274

Goldman, A., Brunn, H., and Ackerman, L.: Tuberculous cavities 275

Wiese, E. R.: Spontaneous closure of tuberculous cavities 275

Shamaskin, A.: The inspissated cavity 275

Paine, A. L.: Bilateral tuberculous pleural effusions 276

Meleney, H. E.: Pulmonary histoplasmosis . 276

Chapman, J., and Smith, H. E.: Diameters of normal and abnormal bronchi 277

Chapman, J., and McCullough, D.: Classification of chronic bronchiectasis 277

Chapman, J., and Hoskins, H.: Bronchiectasis 277

Cohen, S.: Lympho-haematogenous tuberculosis 278

Weidman, W. H., and Kieffer, J.: Laminagraphy in chest conditions 278

Smith, A. B., and Bowser, J. F.: Spontaneous pneumomediastinum (mediastinal emphysema) with reports of two cases in infants 279

Neely, J. M.: Idiopathic cardiac enlargement occurring in infants and children 279

Garland, L. H., and McKenney, A. C.: The roentgen diagnosis of vitamin-deficiency cardiac conditions 280

Baylin, G. J.: Patent interauricular septum associated with mitral stenosis: Lutembacher's syndrome 280

Kampmeier, R. H., and Jones, E.: Esophageal obstruction due to gummata of esophagus and diaphragm 281

Fuhrman, M., Dragutsky, D., Rook, G., and Grossman, L.: Congenital atresia of esophagus 281

Abdomen

Hardt, L. L., and Cohen, S. J.: Gastrointestinal complications in pulmonary tuberculosis 281

Bruck, S., and Fruchter, J. M.: Influence of a single dose of commonly used laxatives on gastro-intestinal motility 282

Garland, L. H., and Brown, J. M.: Roentgen diagnosis of spontaneous internal biliary fistulae, especially those involving the common duct 282

Ortmayer, M., and Connelly, M.: Star-shaped radiolucencies of gallstones: a rare roentgen sign 282

Joffe, H., and Wachowski, T. J.: Relation of density of cholecystographic shadows of gallbladder to iodine content 283

Gordon, J. S., and Manning, J. J.: Autopsy survey of gastro-duodenal ulcers in Philadelphia General hospital 283

Chont, L. K.: Phytobezoar and its formation in vitro 283

Beling, C. A., Baker, C. F., and Marquis, W. J.: Pancreatic calcification 283

Ritvo, M., and Hewes, F. L.: Clinical roentgen manifestations of carcinoma of duodenum 284

Rendich, R. A., Poppel, M. H., and Cove, A. M.: Roentgen diagnosis of space-occupying lesions in region of head of pancreas 284

Mattingly, D., and Menville, L. J.: Abdominal pregnancy 284

Gynecology and Obstetrics

Leventhal, M. L., and Solomon, E. M.: Therapeutic value of tubal patency tests in sterility and infertility 285

Bray, P. N.: Fetal motion factor in roentgenographic diagnosis of pregnancy 285

Morton, D. G., and Hayden, C. T.: Comparative study of male and female pelves in children with consideration of etiology of pelvic conformation 286

MISCELLANEOUS

Bach, E.: Question of injury to patients and personnel from roentgen rays 286

Stenstrom, W.: Elimination of radioactive elements by patients and rabbits after injection of thorotrast 286

Marinelli, L. D., and Kenney, J. M.: Absorption of radiophosphorus in irradiated and non-irradiated mice 287
Kenney, J. M., Marinelli, L. D., and Woodard, H. Q.: Tracer studies with radioactive phosphorus in malignant neoplastic disease 287
Zahl, P. A., and Cooper, F. S.: Physical and biological considerations in use of slow neutrons for cancer therapy 288
Goldfeder, A.: Further studies on effects of irradiation on proliferation and metabolic processes of normal and malignant mammalian tissues 288
Ellinger, F., and Gross, R.: Depth dosage measurements by means of goldfish 288
Potter, J. C.: Biological effect of roentgen rays of long and short wavelength on totally irradiated rat 289
Chaoul, H., Schatter, T., and Wachsmann, F.: Fundamentals in dosimetry in close irradiation 289
Happey, F.: Construction of universal dosemeter 289
Schönander, G.: Study of secondary screening 290
Stanford, B.: Research into physical factors concerned in indirect radiography 290
Harvey, R. A.: Rapid dark adaptation test .. 290
Blonek, F.: Universal table for fluoroscopic localization of foreign bodies 290
Corby, R. A.: New Method of localization by modified use of laminagraph 291
Teperson, H. I.: Simple film-drying shelf for dark room 291
Sussman, M. L., Steinberg, M. F., and Grishman, A.: Rapid film changer for use in contrast angiocardiography 291
Erf, L. A.: Note on effect of dermal and enteral irradiation by radio-phosphorus on blood levels of dogs 291
Janzen, A. H., and Warren, S.: Effect of roentgen rays on peripheral nerve of rat. 292
Evans, T. C., Goodrich, J. P., and Slaughter, J. C.: Temperature and radiosensitivity of skin of new-born rats 292

ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

Grant, Francis C., Webster, John E., and Weinberger, Laurence M. Unusual symptomatology with tumors of the cerebellum based on 158 verified cases. *Am. J. M. Sc.*, Sept., 1941, *202*, 313–329.

The authors discuss 158 cases of tumors of the cerebellum seen in the Neurological Service of the Hospital of the University of Pennsylvania. They give the usual findings in tumor of the cerebellum and point out unusual findings which may confuse the diagnosis.

The tonic cerebellar fit has been recognized as the characteristic type of convulsion in tumor of the cerebellum but various types of convulsion ranging from this to typical clonic convulsions may occur, due to changes in the flow of blood to the cerebellum caused by changes in the relationship between intracranial pressure and systolic blood pressure.

Visual fields defects are unusual in tumor of the cerebellum but they may be caused by a distended third ventricle and therefore their presence does not exclude this form of tumor. False localizing signs may also be produced by increased intracranial pressure which also cause confusion.

Papilledema was absent in 15 of these cases. This is not unusual if the cranial sutures are widened. But 12 of these cases were in patients more than twenty years old and absence of this symptom is confusing. There was a high incidence of decrease or absence of vision, and visual hallucinations occurred in 8 cases.

Nystagmus is considered an important sign of disease of the cerebellum but it was absent in 41 of these cases and 18 showed vertical nystagmus.

Lumbar puncture was performed in 50 of the cases without any bad effects. The spinal fluid and pressure were normal in 11 cases. Earlier diagnosis of tumor of the cerebellum may account for hospitalization of patients before increased pressure has developed. Apparently neither normal spinal fluid pressure nor absence of papilledema rules out tumors of the cerebellum.

About a third of the patients in this series showed roentgen signs of increased pressure. In addition, there was calcification of the tumor in 2 cases, rarefaction of the bone overlying the tumor in 3, erosion of the petrous ridge in 3 and

parasellar lesions in the right middle fossa in one. There was ventriculographic evidence of tumor of the posterior fossa in 21 out of 37 cases examined in this way. This method is used only in cases in which the diagnosis is obscure.

Sensory disturbances were not unusual. Caloric examinations which were carried out in 41 of the cases were misleading in 5, in which they suggested a lesion above the tentorium. The findings were normal in 9 cases. It was found that the tendon reflexes have little localizing value in tumors of the cerebellum. Cranial nerve palsies were frequent and in a number of cases confirmed the diagnosis.—*Audrey G. Morgan.*

EPSTEIN, BERNARD S. Skull laminagraphy. *Radiology*, Jan., 1942, *38*, 22–29.

Laminagraphy is a method of making roentgen examination of definite layers of a structure. It has been used extensively in examination of the chest. The author describes its use in the examination of the skull in both normal and pathological cases. He used an Alexander apparatus and made laminagrams at depths of 2.5, 5.0 and 7.5 cm. As a rule the 7.5 cm. plane corresponded to the center of the skull. Four cases with pathological lesions are described and laminagrams given of the normal skull at the various depths and of cases with frontal and parietal meningioma, meningioma of the right frontal lobe with hyperostosis of the overlying bone and of osteoma of the frontal sinuses. —*Audrey G. Morgan.*

PEYTON, WILLIAM T., and PETERSON, HAROLD O. Congenital deformities in the region of the foramen magnum: basilar impression. *Radiology*, Feb., 1942, *38*, 131–144.

Basilar impression is a rare anomaly, though minor changes around the foramen magnum and upper part of the cervical spine are quite frequent. In basilar impression the foramen magnum is irregular in outline, smaller than usual with its margins directed upward into the skull. The downward slope of the clivus is decreased; its trough is broad and flat, and the petrous portion of the temporal bone is pushed upward. The floor of the posterior fossa is thin and there is a variable degree of fusion of the atlas with the occipital bone.

Patients with this anomaly have a short neck and an abnormal position of the head with limitation of head movements. There may or may not be neurological symptoms. If there are they generally do not appear until after adolescence but they are progressive and often fatal. The neurological signs are irritation and paralysis of cervical nerves and spinal cord tracts caused by compression at or near the foramen magnum; irritation and paralysis of the cranial nerves in the posterior fossa; compression of the medulla oblongata by the odontoid process, cerebellar disturbances caused by compression of the cerebellum in the shallow posterior fossa and increased intracranial pressure.

The most common roentgen findings are absence of the posterior arch of the first cervical vertebra and the high position of the odontoid process which is somewhat displaced backward. A lateral view of the cervical spine and base of the skull shows these changes. An effort should also be made to demonstrate the foramen magnum and the fusion of the atlanto-occipital joints.

Twenty-six cases from the literature are reviewed and 3 new cases described. Basilar impression has heretofore been considered hopeless but recently some cases have been treated by suboccipital craniotomy and laminectomy of the upper cervical vertebrae. So far the results have not been extremely good but the cases have been too few and too recent for definite judgment to be passed on its value. It is not to be expected that nerve tracts that have undergone compression for years could be restored but if the operation prevents progression of the disease and death it is very much worth while.—*Audrey G. Morgan.*

NECK AND CHEST

DUNCAN, ROBERT E. Pulmonary tuberculosis; its exclusion from the Navy. *Am. Rev. Tuberc.*, Dec., 1941, *44*, 651–657.

The problem of pulmonary tuberculosis has always been considered a serious one by the United States Navy, but it now appears to be unusually important considering that the cruising range must be so much greater than formerly, requiring close quartering of men for long periods of time.

Sailors like to consider themselves hardy and, since the onset of tuberculosis is so insidious, spread of the infection may take hold before any knowledge of a case. Moreover, much tropical and subtropical service is required, where active lesions spread rapidly and poorly healed lesions break down.

Therefore, any evidence of activity or any

evidence of a reinfection process serves to disqualify a man from service in the Navy.

Roentgenography is considered to be the most reliable method of detecting poor risks. The several methods of roentgenographic procedure are discussed, with the conclusion that the 35 mm. film is most practical for the Navy. Two hundred to 500 examinations can be accommodated per day—a maximum of 80 per hour. However, this procedure is considered to be merely a screening process, allowing supplemental studies with the use of 14×17 inch films. At Norfolk, these collateral studies were called for in approximately 1 to 2 per hundred.

The following evidence was considered disqualifying:

1. Any evidence of reinfection (adult) type tuberculosis, active or inactive, exclusive of slight thickening of the apical pleura.
2. Evidence of active primary (childhood) type tuberculosis.
3. Inactive primary pulmonary tuberculosis if the degree or extent of involvement appears to be of present or future clinical significance.
4. Evidence of fibrinous or serofibrinous pleuritis.

Some application of this method is being utilized for first study of those already in the service and a few cases of active pulmonary tuberculosis have thereby been discovered.

In 1938, the admission rate for tuberculosis in the Navy was 0.87 per thousand while the non-effective rate was 0.65 per thousand. In 1939, the admission rate was 1 per thousand, and the non-effective rate 0.65 per thousand.—*A. A. de Lorimier.*

de Lorimier, Alfred A. Mass roentgenography of the chest for the United States Army. *Radiology*. April, 1942, *38*, 462–472.

It is very important that thorough examinations be made of the chests of all Army recruits and that records of them be kept, both from the point of view of preventing dissemination of the disease and of preventing claims being made against the Government for disabilities not acquired in the service. The present methods of mass roentgenography are much more effective than the physical methods used in World War I.

Various methods of making mass examinations are discussed and the technical details compared. Taking into consideration various features, such as reliability for the study of a single case, reliability for mass studies, coordination with physical examination, durability, the problem of storage and cost, it would seem that the best method is the stereoscopic viewing of 4×5 inch films. Special stereoscopic viewing units are now available.

Apparently the most practical milliamperage is 200. This necessitates a generating unit with full-wave rectification and a capacity of not less than 200 ma. at potentials as high as 100 kv. (peak). When examining for the Army, exposures must be made at the rate of one or two per minute which involves severe strain on the tube. It must be able to withstand as much as 700,000 heat units per hour. This makes it necessary to use stationary anode tubes. Single emulsion films are better than those with a coating of emulsion on both sides as they prevent blurring and decrease contrast. Excessive contrast may also be prevented by using kilovoltages higher than those usually used for chest examinations—80 to 90 or even up to 100 kv. (peak) instead of the usual 60 to 70. A stationary or wafer grid has been constructed for the Army with which the grid marks are not conspicuous or even visible. The best focal-screen distance is 36 to 48 inches. With less than 36 inches there is distortion and with more than 48 there is apt to be loss of detail from motion due to the longer exposure time required.

When as many as 200 to 400 examinations are being made a day there is danger to the technicians unless they are protected with lead shields.—*Audrey G. Morgan.*

Pollock, William C. Tuberculosis in the Army; the tuberculosis problem of World War No. 1 and in the present mobilization. *Am. Rev. Tuberc.*, Dec., 1941, *44*, 658–674.

During the last great mobilization, in 1917, the Surgeon General of the Army was advised by the Medical Committee of the Council of National Defense to make chest examinations of each candidate for the Service. These were accomplished by specialists. Films were not used. Six hundred physicians participated in examining 3,288,669 men of whom 22,596 were rejected because of pulmonary tuberculosis. Upon demobilization, an additional 1,356 were detected among more than 2,000,000 expeditionary forces sent to France (8,717 were returned to the United States with the clinical diagnosis of pulmonary tuberculosis).

Various congressional enactments have nullified excellent work by various tuberculosis boards which attempted to protect our Government.

In 1917, many authorities clearly disfavored the use of roentgenography in conducting examinations of the chest, describing its deficiencies in words such as the following: "Morbid changes in the lungs are shown by shadows due to two substances: First, blood, second, fully organized connective tissue. Tubercle caseations, as such, cast no shadows distinguishable from other tissues of the parenchyma. We do not see tubercles in the x-ray negative. What we see are either sharply outlined calcifications and fibroses, or fuzzy congestions, or a combination of the two conditions. Frequently the tuberculous process runs so chronic a course that the inflammatory reaction is insufficient to congest the lung enough to produce a shadow."

The mobilization survey of 1941 is considered to be the greatest "case finding effort ever carried out in this country." The usual program of detection has been unsatisfactory because studies have been made following induction and the inductees have been discharged to their own care.

The mounting costs of compensation are exemplified with figures such as the following: in 1923, the cost of compensation for tuberculosis was $32,658,360 while in 1940 it was $35,018,820. In 1940 there were 849,298 veterans on the pension rolls with an annual cost of $254,486,260.

Statistical charts are presented showing deaths due to tuberculosis by age groups in percentage of all deaths; the tuberculosis rate per 1,000 in the Philippines, the United States and Hawaii; monthly compensation costs for tuberculosis during the years 1923–1940 and veteran costs for the War of 1812 and each war in which the United States has engaged thereafter.

Roentgen examinations are advocated but a warning is cited that these studies serve to eliminate tuberculosis only for the moment; activity may develop soon after induction.—*A. A. de Lorimier.*

Hodges, Fred Jenner. Fluorographic examination of the chest as a routine hospital procedure. *Radiology*, April, 1942, *38*, 453–461.

The University of Michigan has adopted the plan of making routine chest examinations of all patients admitted to the hospital, using the method of photofluorography, or photographing fluoroscopic screen images on sensitive film of reduced size. Though their apparatus was homemade and did not include provisions for stereoscopy nor a stationary grid for the elimination of excessive scattered radiation, they found roentgen signs sufficiently serious to indicate further careful examination in more than 8 per cent of the patients. Technical improvements will doubtless increase the accuracy and usefulness of the method.

Of course the survey plan will not detect every case of intrathoracic disease nor will it take the place of methodical physical examination. But used as a screen to detect cases needing further examination it is of great value and it is perhaps of more value in detecting advanced than minute beginning lesions. With careful planning it can be carried out in general hospitals without overburdening the roentgenological department.

Its use as a routine method in admitting patients is analogous to that of routine urine examination and routine Wassermann tests. In the author's experience routine serologic tests have given positive results in about 2 per cent of the cases while chest surveys have shown significant changes in more than four times that number.—*Audrey G. Morgan.*

Pindell, M. L. Photoroentgenography in a tuberculosis program. *Radiology*, Feb. 1942, *38*, 224–231.

The author describes the work in photographing the images from 4×5 inch films used in the mass examination of patients at the East Los Angeles Health Center. By the use of this method the output of the center has been increased about 50 per cent and costs have been reduced proportionately. Storage space has been reduced at least 65 per cent. They have found the 4×5 inch film superior to the 35 mm. film. If any suspicious shadows are seen on the film it is duplicated on a regular 14×17 inch film. So far they have made 6,000 exposures on 4×5 inch films and have not had any great difficulty in their use.

He believes that miniature films made and interpreted by experienced roentgenologists will become of increasing importance in the mass examination of draftees, for example, in detecting new cases of tuberculosis.

The General Electric X-ray Corporation has just perfected a stereoscopic attachment for these units which utilizes a 4×10 inch film and gives a true stereoscopic effect. But a special

stereoscope is required to view the films. This new stereoscopic assembly will doubtless prove valuable in examination for tuberculosis.—*Audrey G. Morgan.*

Goldman, Alfred, Brunn, Harold, and Ackerman, Lauren. Tuberculous cavities; observations on transpleural decompression. *Am. Rev. Tuberc.*, Feb., 1941, *43*, 151–183.

Collapse therapy is essentially cavity therapy. The physiological changes concerned with such treatment were studied in 7 cavities by way of cavernoscopic examinations supplanted with bacteriological and roentgenographic studies.

Pathological and cavernoscopic studies revealed, frequently, tissue flaps and exudate serving to produce a ball-valve effect, air being allowed ingress but exhalation of it being inhibited.

Bronchoscopic studies of the cavities revealed edema, injection, and occasionally tubercles, polypi, ulcers and hard and soft localized stenoses. They indicated a definite relationship of bronchial lesion to the development of cavitation. Some of the bronchi showed elongation; others, narrowing, tortuosity or other malformations. Bronchial obstruction appeared to be of lesser degree following artificial pneumothorax than following thoracoplasty.

Kymographic tracings were made of the intracavity pressures under various conditions. Seldom was the pressure found to be related to in-and-out breathing of the cavity. Ordinarily, intracavity pressures are usually less than 10 cc. of water. They may become elevated to plus 18 or as much as plus 24 cc. water by transpleural injection of air. Still, drainage does not always occur. Eventually, complete obstruction of draining bronchi was noted in all of the cases studied. Non-tension cavities were found to have flow of air in and out.

Transpleural decompressions were attempted in 20 cavities (18 patients). Seven of these were incomplete either because of failure of cooperation or because of apparent aggravation. There were 3 deaths.

The mechanism of healing of cavities is considered to ordinarily involve three phases: (1) stabilization of the intracavity pressure at or below atmospheric pressure (a physical effect); (2) disappearance of tubercle bacilli (bacteriological effect), and (3) conversion of the cavity into a fistulous tract (pathological effect).

These studies indicate that compression therapy produces benefit chiefly by way of neutralizing the harmful effects of respiratory trauma—i.e. by stabilization of pressures. Poor results may occur if bronchus-to-cavity valve mechanisms are so efficient that they continue to allow high pressures and fluctuations of pressure to exist within the cavities.

Activity of the tubercle bacillus does not seem to be responsible for the maintenance of cavitation (this, in accord with Coryllos).—*A. A. de Lorimier.*

Wiese, E. Robert. Spontaneous closure of tuberculous cavities. *Am. Rev. Tuberc.*, July, 1941, *44*, 92–93.

Of 125 cases of pulmonary tuberculosis with cavitation suitable for study, 20 (16 per cent) showed spontaneous closure with no treatment other than bed rest. The criteria considered to indicate closure included disappearance of the outlines of the walls together with disappearance of the area of rarefaction, as revealed roentgenographically, and clinical improvement of the patient. All of these cases were considered unfavorable for collapse therapy. In all instances, the walls of the cavities were thin. In most, the involution was gradual with the development of fibrotic deposits, though in one case there was no discernible scarring.—*A. A. de Lorimier.*

Shamaskin, Arnold. The inspissated cavity. *Am. Rev. Tuberc.*, Sept., 1941, *44*, 310–322.

The mechanism of cavity closure likely varies. In some cases, closure of the drainage bronchus may be a factor for obliteration of the cavity. However, this factor may produce an opposite effect—actually preventing cavity obliteration.

Various observers have noted a lack of communication between cavities and the tracheobronchial tree, though Auerbach and Green have emphasized that they have never seen a cavity of 3 cm. in diameter or larger without being able to find a communicating bronchus.

Six cases of inspissated cavities are described. These were all characterized by intermittent filling, partial emptying with the development of fluid levels and with eventual healing after a period of years. Healing was considered to imply clearing of the parenchyma

regional to the lesion, obliteration of the area of rarefaction and disappearance of tubercle bacilli from the sputum. Occasionally, involution was evident roentgenographically, on one side, even though progression of the pathologic condition occurred in the opposite side. Certain cases showed evidence of filling of cavities without there being any clinical manifestations of toxicity, while others manifested considerable fever and toxicity with the same roentgenographic evidence. This is explained on the basis of the character of the contents of the cavities—it being conjectured that lack of toxicity may signify tissue content rather than sputum and active bacterial culture.

An inspissated cavity may be mistaken for an area of caseous bronchopneumonia. However, the latter cannot be expected to become as sharply outlined as in the case of a tissue inspissated cavity (the former being the seat of active disease rather than retrogression).

This type of cavity may be confused with metastatic neoplasm. Metastases are usually multiple and, with them, a primary lesion can usually be identified.

As for treatment, collapse therapy appears to be indicated for those cases which show opening and closing. Not infrequently, these cavities are not benefited by this type of treatment. This may be due to excessive fibrosis or to the improper selection of time for the treatment. Collapse should be instituted only during the stage of open bronchial communication. Frequent roentgenographic studies may be necessary to determine both the identity of an inspissated cavity and the opportune time for collapse of it.—*A. A. de Lorimier.*

Paine, Alfred L. Bilateral tuberculous pleural effusions. *Am. Rev. Tuberc.*, Oct., 1941, *44*, 424–438.

Forty-five cases of bilateral pleurisy were studied in the Manitoba Sanatorium. It appeared that bilateral involvement indicated a much more serious condition than did unilateral. Reinfection parenchymal lesions developed in higher incidence in the former group, as did also lesions in organs other than the lungs. Five of the cases showed miliary lesions and most showed lesions in one or more locations, including the spine, kidneys, adrenals, lymph nodes and meninges. Thus, it appeared that bilateral effusion may signify hematogenous infection and it may indicate a generalized miliary tuberculosis. In contradistinction, unilateral effusions generally appeared to represent extensions of a subpleural lesion originating from aerogenous infections. The effusion itself was considered to manifest an allergic reaction—as suggested by Boyd.

Localization of tubercle bacilli in the pleura is common to hematogenous infections. This has been explained on the basis of the vascular transition zone located between the bronchial vascular bed (which supplies the pleurae) and the vascular bed concerned with the pulmonary vessels themselves (which supply the parenchyma). From this zone, infections may easily extend either outwardly or inwardly. Ten of 17 cases of miliary tuberculosis showed these extensions.

The author is perplexed with the consideration of unilateral allergy and delay in reactions on one side versus the other; as to why many cases of unilateral pleural involvement fail to manifest any parenchymal lesions and vice versa, and finally why many subpleural parenchymal lesions fail to manifest pleural reactions. Further investigation appears indicated.—*A. A. de Lorimier.*

Meleney, Henry E. Pulmonary histoplasmosis. *Am. Rev. Tuberc.*, August, 1941, *44*, 240–247.

Histoplasmosis (Darling) or "reticulo-endothelial cytomycosis" is a disease of protean manifestations. During the acute stage it is a systemic infection involving the reticulo-endothelial cells just as in the case of kala azar. It has been manifested as a chronic skin disease or as a disease involving the mucous membranes essentially, or the lymph nodes, or the adrenal glands or the lungs. It has been recognized in the dog and ferret. Most cases have been recognized only after microscopic studies. It may simulate tuberculosis and it may occur concurrently with tuberculosis.

Two cases are presented. Roentgenographically, the first showed multiple, sharply circumscribed densities in both lungs—interpreted as metastatic malignancy. There were extensive fibroses at both bases. These lesions expanded and the patient died approximately six weeks following the first evidence of a pathological condition of the chest. Postmortem examination revealed thickened pleurae, parenchymal consolidations and fibrinous exudate. Mononuclear cells were numerous and

they were filled with round or oval parasites averaging about 3 microns in diameter. In the parenchyma, the nodulations consisted of a central caseous region, oftentimes broken down into a cavity and containing amorphous substance and nuclear fragments. In some of the smaller caseous areas, acid-fast bacilli were found, these resembling tubercle bacilli. In the liver and spleen, similar nodular areas were found but there was no evidence of parasitized cells in these, though acid-fast bacilli were found in some. These were definitely considered to be tubercle bacilli. Their dissemination is explained on the basis of lowered resistance.

The second case was featured by a long period of night sweats—attributed to a bladder stone and urinary tract infection. He had lost 16 pounds in six months and was definitely emaciated. In addition to the findings of urinary tract infection, he was found to have cavities at the apices of both lungs. The sputum contained acid-fast bacilli. Following a cystotomy, he developed a bloody diarrhea, cough, hemoptysis and an ileus—with which he died. Postmortem studies revealed *Histoplasma capsulatum* in macrophages located at the edges of the cavities in the lung. Apparently, histoplasmosis was at least partially concerned with what otherwise appeared to be caused by tuberculosis.

The author suggests that this fungus may act as a collateral infection or it may act as a sole invader but that it will likely be found associated with many cases, when it becomes better known. Since it has been discovered both in man and in animals, it may be transmitted from one warm blooded host to another.—*A. A. de Lorimier.*

Chapman, John, and Smith, Howard E. Diameters of normal and abnormal bronchi. *Am. Rev. Tuberc.*, April, 1941, *43*, 504–511.

This study was based upon approximately 200 bronchograms. All were made at the end of deep inspiration. Measurements of lower lobe bronchi were selected. Levels were identified in relation to main stems.

No significant difference could be found with respect to the two sides nor between sexes, for any one level. Significant changes were noted in bronchiectasis. Slight variations were found with a direct relationship to body weight. Likewise, there was a slight direct proportionality between transverse thoracic diameter and bronchial diameter.

In the case of bronchiectasis, the variations were only slight in the upper portions of involved bronchi but they were very appreciable at the more distal levels.—*A. A. de Lorimier.*

Chapman, John, and McCullough, David. Classification of chronic bronchiectasis. *Am. Rev. Tuberc.*, April, 1941, *43*, 521–526.

The authors are proposing the following classification of bronchiectatic lesions:

I. The Etiological Factor
   - A. Congenital
   - B. Primary bronchiectasis
   - C. Acquired or secondary bronchiectasis: postpneumonic, postbronchopneumonic, influenzal, postabscess, sinus-bronchitic form of Ochsner, mixed etiology, bronchiectasis as as a sequel to or in association with specific thoracic disease (tuberculous, fungous, malignant, silicotic).

II. The Anatomical Factor
   - A. As to morphology of dilatation: cylindrical, saccular, varicose, fusiform, bronchiolectasis, mixed forms.
   - B. As to location: according to lobes, right middle, right lower, left upper, etc., according to bronchus, lingular, medial axillary, basilar, etc., following the nomenclature of Peirce, as to extent (diffuse, circumscribed).
   - C. As to degree of dilatation: slight, moderate, severe.
   - D. As to associated pathology: with abscesses or cysts, with atelectasis, with stenosis.

III. The Functional Factor
   - A. Symptomless
   - B. Dry, hemoptoic (Sicard and Forestier)
   - C. Mild productive
   - D. Severe productive
   - E. Septic

IV. The Prognostic Factor
   - A. Progressive
   - B. Nonprogressive
   - C. As to health and life

It is admitted that atelectasis must also be considered as an etiological factor.—*A. A. de Lorimier.*

Chapman, John, and Hoskins, Henry. Bronchiectasis. *Am. Rev. Tuberc.*, April, 1941, *43*, 512–520.

Most writers have considered cylindrical dilatations of bronchi to be the mildest form of bronchiectasis. Bronchosinusitic disease is generally considered relatively mild, while bronchiectasis resulting from acute suppurative pneumonias is likely to be of severe degree. A

"beaded" or "varicose" form has been described—this being featured by transverse ridges. Other types of lesser incidence include dilatations of the smaller branches such as may develop following influenza.

The authors have studied 116 cases in the State Tuberculosis Sanatorium (Texas), in this regard. They have limited their classification to cylindrical (60 cases), saccular (26 cases) and varicose (24 cases) types, disregarding fusiform (4 cases) and bronchiolectatic (2 cases) because of the low incidence of the latter.

Cylindrical types were found about twice as frequently as either of the other two. Approximately two-thirds of the cases were females (but approximately two-thirds of the hospital cases were females). Less than half of the entire group had noted hemoptysis. Of these, 20 per cent had noted blood streaked sputum; the rest claiming frank blood spitting. Complete absence of hemoptysis was more common to the cylindrical type than to the saccular or varicose types. About 42 per cent claimed profuse expectoration for more than two years. About 40 per cent denied ever having had pneumonia (about 50 per cent of the cylindrical group denied it, approximately 77 per cent of the saccular had the disease one or more times and 63 per cent with the varicose dilatation had record of it). Only 35 per cent of the entire group admitted having any type of disease of the nose or paranasal sinuses. The only patients known to have had asthma fell into the cylindrical group. Otherwise there were no typical findings though the cylindrical types failed to show any physical signs more often than did either of the other two types.

Of 100 cases studied by complete injection on both sides, 39 had bilateral disease; 34, changes in the right lower lobe and 27, in the left lower lobe.—*A. A. de Lorimier.*

Cohen, Samuel. Lympho-haematogenous tuberculosis. *Am. Rev. Tuberc.*, May, 1941, *43*, 612–627.

Tuberculosis is too often considered as a localized pneumonic infection.

This study deals with 426 cases studied at the Jersey City Medical Center. Seventy-eight per cent were white; 22 per cent, colored; 55.6 per cent, males; 44.4 per cent, females; 18.3 per cent showed evidence of lympho-hematogenous spread of the disease.

The acute or subacute cases showed miliary lesions in the lungs and 5 of the 7 developed meningitis; 3 had associated pleural effusions; 2 had palpably enlarged spleens. Among those classified as chronic (4 patients) the duration of symptoms varied from two to twelve years. These showed roentgen evidence of lesions (3, bilateral symmetrical seedings and later, irregular enlargements); 3 had superficial adenopathy and 2, pleural effusions; 2 showed enlarged spleen. Otherwise, the essential findings were: meningitis, Pott's disease, arthritis, epididymitis and calcified abdominal lymph nodes.

There was only 1 case of subacute or chronic medium-sized nodular hematogenous lesions. It was characterized by confluence of the metastatic lesions and considered as intermediary in transition from hematogenous to truly bronchogenic disease—though it was interrupted by a meningitis.

There were 17 cases of protracted hematogenous multiform lesions—including 1 case of sarcoid. In these, it appeared that the toxic and bacillary implantations occurred in successive crops, over periods of months, thereby producing lesions of varying size and age. Notable findings included multiple serositis, widespread adenitis and splenic enlargement.

Nine cases showed progression of the lesions with ultimate cavity formation, bronchogenic spread and positive sputum. These were described as protracted multiform types.

Sixteen of the cases showed phthisis at the time of admission with positive sputum in all but one. These later developed hematogenous spread to the meninges, epididymis, prostate, female adnexa, knee, spine, humerus or clavicle. The average duration of symptoms was two and one-half years.

However, the author hopes that he has "not conveyed the impression that hematogenous dissemination ends fatally."—*A. A. de Lorimier.*

Weidman, William H., and Kieffer, Jean. Laminagraphy in chest conditions. *Am. Rev. Tuberc.*, Feb., 1941, *43*, 202–212.

Too many reports pertaining to the use of laminagraphy have been concerned only with spectacular aspects.

The authors have analyzed the merits of this procedure in a comparative way. Their cases were studied by conventional stereoscopic roentgenograms, by fluoroscopic examination

and by an overexposed posteroanterior projection using a Lysholm grid, all prior to laminagraphy. Routinely, the Kieffer parabolic spiral motion was applied in a few instances; the results were compared with rectilinear and circular laminagraphic motions.

It was soon felt that fluoroscopy provided only meager information and that procedure was therefore discontinued (mainly to avoid excessive radiation exposures).

The laminagraphic exposures were made for axis levels varying at 1 cm. but 1.5 cm. steps appeared practical for many cases. Since most of the lesions warranting this study are located posteriorly, the patient was usually placed in the supine position. Preliminary Potter-Bucky studies were made and close cooperation between doctor and technician was exercised.

In scouting for the proper level of sectional studies, it is suggested that the first exposure be made at 1 cm. posterior to the mid-plane of the anteroposterior chest diameter. This usually visualizes the bifurcation of the trachea. The authors then proceeded to take three central films made at levels 1 cm. apart, the remainder being made at levels 1.5 cm. apart, extending from 4 or 5 cm. anterior to the very posterior plane of the thorax to about 13 or 14 cm. therefrom.

An apex study usually required three or four films (8×10 inch); a thoracoplasty case, about 7. It was found that laminagrams taken below 5 cm. or over 14 cm. were seldom of any value.

After experimenting with various focal film distances, 90 cm. appeared practical and became used routinely. The milliampere-seconds varied from 40 to 160 (10 ma. at 4 sec. to 20 ma. at 8 sec.) while the peak kilovoltage was varied from 52 to 82. It was found that the factor of respiration was definitely important because of variations in the position of a lesion during inspiration as compared with expiration. Likewise, positioning of the head was found to alter relations; therefore, it was supported to the mid-position. Study of the films must be made in an orderly manner, preferably following the same order pursued for the laminagraphy. Cavities are visualized as sharply outlined circles (i.e. when using the spiral motion) or as rectangular densities.

Sectional studies are necessarily expensive but they frequently visualize lesions which otherwise are unsuspected. In particular, they serve to reveal densities ordinarily obscured by the density of the scapula or the cardiac silhouette and even small lesions in the trachea or bronchi. Moreover, they provide for localization of such lesions. They contribute to the value of lipiodol studies and serve to clarify detail in cases of compressed lung tissue. In cases of empyema they may reveal more than visualized with the use of lipiodol.

For early cases of pulmonary tuberculosis, sectional studies alone are not recommended.

An analysis of 100 cases, comprehensively studied, indicated that the sectional studies provided: no gain in 18 per cent; definite value (not entirely unsuspected), in 36 per cent, and "unsuspected information" in 40 per cent.—*A. A. de Lorimier.*

Smith, Arthur B., and Bowser, John F. Spontaneous pneumomediastinum (mediastinal emphysema) with reports of two cases in infants. *Radiology*, March, 1942, *38*, 314–319.

The literature on spontaneous pneumomediastinum is reviewed and two new cases reported, both in newborn infants. There was recovery with spontaneous absorption of the air in both cases. This condition should be considered in infants with cyanosis and dyspnea, rapid pulse and congestion of the vessels of the neck, as relief of the increased mediastinal pressure may save life. The diagnosis can be made from a lateral roentgenogram of the chest. Air can sometimes be seen in the negative between the layers of the cervical fascia before there are any clinical signs.

In adults spontaneous pneumomediastinum usually follows wounds of the chest or therapeutic pneumothorax. The symptoms may be so severe as to stimulate those of coronary occlusion but there is no shock or weakness of the myocardium. There may be a crackling bubbling sound over the heart on each contraction, caused by compression of the air-filled mediastinal tissues between the heart and the anterior wall of the chest. The diagnosis is confirmed by the appearance of air in the subcutaneous tissues of the neck.—*Audrey G. Morgan.*

Neely, J. Marshall. Idiopathic cardiac enlargement occurring in infants and children. *Ann. Int. Med.*, Oct., 1941, *15*, 727–742.

Congenital idiopathic cardiac hypertrophy is a name that has been applied to enlargement of

the heart in infants and young children for which no cause can be found. It is probable that as more careful examinations are made fewer and fewer cases will be classified as idiopathic. Some cases formerly so diagnosed have already been shown to be caused by enlarged liver with glycogen infiltration of heart, liver and kidneys, and some occur in sickle cell anemia.

Three cases are described in children twenty-five days, eleven months and three years of age. Roentgenograms are given and photomicrographs of heart and liver tissue. In all of these cases the enlargement of the heart was secondary to chronic interstitial pneumonitis. In the boy three years of age, the pneumonitis had brought about chronic pulmonary emphysema as a compensatory change. This adds to the load on the right heart.

In all these cases there was dyspnea, cyanosis, rapid pulse and enlargement of the heart, predominantly on the right. Persistent fine mottling of the lung fields in cases of enlarged heart which persist in spite of treatment for decompensation indicates chronic interstitial pneumonitis as a possible cause of the enlargement of the heart.—*Audrey G. Morgan.*

Garland, L. H., and McKenney, A. C. The roentgen diagnosis of vitamin-deficiency cardiac conditions. *Radiology*, April, 1942, *38*, 426–444.

Certain types of vitamin deficiency are often associated with enlargement of the heart. They are probably not of great importance except in impoverished share-cropper and slum districts but they will probably be seen in increasing numbers after the war as a result of famine conditions. Probably the most frequent cause of these heart conditions is thiamin deficiency. It is not stored as well as the other vitamins and leaves a smaller reserve for periods of deprivation. In these cases the heart is enlarged and the pulse slowed. As a general rule, there is prompt and satisfactory response to thiamin treatment. The signs of heart failure disappear and the size of the heart decreases greatly within two weeks. Very advanced cases may not respond to treatment. These are usually terminal cases or those in which there is added damage to the myocardium from some other cause.

The roentgen findings in enlarged heart from vitamin deficiency are not pathognomonic. But if roentgen examination shows an enlarged heart that contracts poorly with mild pulmonary congestion in an adult who does not have valvular disease it suggests thiamin deficiency, particularly if there is not hypertension. The diagnosis can be confirmed by the therapeutic test.

Fourteen cases of thiamin deficiency in adults in which there was enlarged heart (beriberi heart) are described. Two cases of vitamin C deficiency in adults and 1 in an infant, 5 cases of combined C and D deficiency in infants and 4 of D deficiency alone are reported but there was no abnormality of the heart in these cases. Roentgenograms are given showing the findings in thiamin deficiency and the improvement under thiamin treatment.—*Audrey G. Morgan.*

Baylin, George J. Patent interauricular septum associated with mitral stenosis: Lutembacher's syndrome. *Radiology*, Jan., 1942, *38*, 1–6.

Though patent interauricular septum is quite common only 26 cases of its association with mitral stenosis have been reported in the literature. Since Lutembacher made a collection of these cases the condition has been known by his name.

As with many other congenital heart defects, this one is compatible with long life and fairly good health. The physical findings are not characteristic so it is probable that many cases have never been diagnosed. But it is possible now to diagnose it by roentgen examination.

Two cases are reported, one in a boy of fifteen and one in a woman of thirty-four. Only 2 of the 26 reported cases have been in females. They showed the characteristic roentgen appearance with enlargement of the heart to right and left and prominence of the pulmonary conus. The hilar shadows were enlarged; in some cases they are so much enlarged that they simulate irregular lymph node masses. The right auricle is enlarged and sometimes the left auricle but not the left ventricle. The densities in the hilar and conus regions may be mistaken for intrathoracic tumors but the doubt can generally be cleared up by fluoroscopy and oblique films. In the author's second case there were usually severe symptoms. Direct pressure of the conus on the left recurrent nerve had caused paralysis of that nerve. The left bronchus was also compressed, which had caused decreased aeration of the left lung with over-

aeration on the right; this explained the slight shift of the heart to the left and the polycythemia.—*Audrey G. Morgan.*

Kampmeier, R. H., and Jones, Edgar. Esophageal obstruction due to gummata of esophagus and diaphragm. *Am. J. M. Sc.*, April, 1941, *201*, 539–546.

Gumma of the esophagus is extremely rare. Four cases of obstruction of the esophagus by gummata seen at the Vanderbilt University Hospital during the past fifteen years are described. In one case the gumma was located in the wall of the esophagus itself, while in the others there was a gumma of the diaphragm which surrounded and constricted the esophagus. In 3 of the cases the correct diagnosis was made and the patients recovered under antisyphilitic treatment. In the other case, in a male Negro, aged sixty-nine, a diagnosis of carcinoma was made in spite of the fact that he was known to have syphilis. He was given roentgen irradiation instead of antisyphilitic treatment and died. Careful study of all the factors in differential diagnosis is necessary in these cases.—*Audrey G. Morgan.*

Fuhrman, Murray; Dragutsky, David; Rook, George, and Grossman, Leo. Congenital atresia of the esophagus. *Radiology*, March, 1942, *38*, 326–329.

The authors describe 2 cases of congenital atresia of the esophagus seen within a month in the maternity service of the Metropolitan Hospital in New York, though none had been seen in the previous ten years with a history of 12,285 deliveries. In both of these cases the upper segment of the esophagus ended in a blind pouch while the lower segment communicated with the trachea. This is the commonest type. Gastrostomy was performed in both cases but in both the infants died. No successful operation for congenital atresia of the esophagus has been reported but with early diagnosis it is hoped such operations will succeed.

The clinical symptoms are typical—constant drooling, frothy mucus in the mouth and pharynx, repeated regurgitation after feeding, followed by coughing, cyanosis and dyspnea. The diagnosis can be confirmed by roentgen examination. Barium should not be used as it is apt to cause fatal bronchopneumonia. Iodized oil is less dangerous but if used it should be removed by suction immediately after the examination is made. The authors suggest the use of aeroesophagography—that is, the insufflation of air into the esophagus through a tube introduced through the nose under fluoroscopic control and the taking of films in the Trendelenburg position.—*Audrey G. Morgan.*

ABDOMEN

Hardt, Leo L., and Cohen, Seymour J. Gastrointestinal complications in pulmonary tuberculosis. *Am. Rev. Tuberc.*, May, 1941, *43*, 628–636.

About two-thirds of the patients admitted to the Municipal Tuberculosis Sanatorium (Chicago) were found to have far advanced tuberculosis, and about 20 per cent, gastrointestinal complaints.

Of 1,000 autopsies (1917–1937) tuberculous lesions of the gastrointestinal tract were noted in 71 per cent, while of clinical studies, approximately 78 per cent were diagnosed as having intestinal tuberculosis. During more recent years, 102 cases were followed both by clinical and postmortem studies. Of these, 92 per cent of those clinically diagnosed were found to have such lesions; 5 were found to have amyloidosis of the liver; 1, a duodenal ulcer; 1, a gastric ulcer.

Gastrointestinal perforations occurred in 23 instances; 2 were in the esophagus; 1, in the stomach; 15, in the intestines and 5, in the appendix. However, since 1935, there was only 1 perforation—this, in the ileum. The reduction in this complication is attributed to better dietary management and in particular, to a smooth, high vitamin, high caloric diet.

Of those autopsied, 4.4 per cent were found to have gastric tumors (2 fibromata of the pylorus, 1 aberrant pancreas and 1 calcified lipoma); 3 showed adenomas of the liver; 2, lipomata of the liver, and 7, hemangiomata. Polyps in the cecum were found in 4; polyps in the colon, in 8; in the sigmoid, in 4; 1 polyp was found in the esophagus.

Of malignant lesions, there were 4 carcinomata of the stomach; 1 of these appeared to be metastatic from the lung. One case showed a metastatic nodule on the duodenum from a carcinoma of the lung. There was 1 malignant tumor of the ileum; 4 carcinomata of the cecum.

Of diverticula, there were 2 gastric, 2 duodenal and 9 Meckel's. Otherwise, there were 3 diverticula in the sigmoid and 1 in the cecum.

Amyloidosis of the liver was found in 162

cases; of the spleen, in 214. In correlation with clinical manifestations, it appeared that amyloidosis increased vomiting and frequently caused diarrhea.

Cholelithiasis was found in 42 cases; cholecystitis with cholelithiasis, in 6 and cholecystitis alone, in 12. Of the latter, 8 had intestinal lesions.

Amebae were not found in any of the cases.

A careful correlation is made of the clinical features with the pathological findings.—*A. A. de Lorimier.*

Bruck, Samuel, and Fruchter, Joseph M. Influence of a single dose of commonly used laxatives on gastro-intestinal motility. *Radiology*, Feb., 1942, *38*, 145–153.

It is important in roentgen examination of the abdomen and lower spine for the intestine to be empty. A study was therefore made of the action of five laxatives on intestinal motility. The laxatives studied were cascara, licorice powder, magnesium citrate, magnesium sulphate and mineral oil. Films were made immediately after the laxatives were given and after one hour, three, four, six, eight, twenty-four and forty-eight hours. Tests of each laxative were made on 3 subjects.

Fluid extract of cascara and compound licorice powder did not cause any change in the emptying time of the stomach. The magnesium salts and castor oil increased it. All of the laxatives caused irritation of the proximal jejunum which lasted for from one to three hours. Magnesium sulphate definitely delayed the passage of the meal through the small intestine; the other laxatives caused a moderate increase in the motility of the small intestine. Of all the laxatives used, compound licorice powder and castor oil brought about the most satisfactory and complete emptying of the colon. They are therefore the best laxatives for emptying the colon in preparation for roentgen examination. —*Audrey G. Morgan.*

Garland, L. H., and Brown, J. M. Roentgen diagnosis of spontaneous internal biliary fistulae, especially those involving the common duct. *Radiology*, Feb., 1942, *38*, 154–159.

Spontaneous internal biliary fistulae are not common, though there are probably more of them than would be suggested by the cases reported. The possibility of their occurrence should always be remembered in making a roentgen examination of the digestive tract. Since the first case was diagnosed by roentgen examination in 1915 ninety cases have been diagnosed in that way.

Ten cases were seen at the San Francisco Hospital between 1931 and 1940. Of these, 7 were examined roentgenologically and 5 of these were correctly diagnosed. An effort was made to differentiate between fistulae between the common duct and intestine and those between the gallbladder and intestine. This differentiation is of some practical importance as the prognosis is good as regards late complications in the former while in the latter it is rather bad. Choledochoenteric fistulae are most commonly caused by rupture of a peptic ulcer from the duodenum into the common duct while the gallbladder type are generally caused by perforation of stones from the gallbladder into the duodenum and stones may later ulcerate through the intestine lower down, particularly in the terminal ileum.

Two of the authors' 10 cases were choledochoduodenal fistulae. They are described and illustrated with roentgenograms. The correct diagnosis was made in one.—*Audrey G. Morgan.*

Ortmayer, Marie, and Connelly, Marie. Star-shaped radiolucencies of gallstones: a rare roentgen sign. *Radiology*, Jan., 1942, *38*, 39–42.

Stellate central fissures were long ago found in gallstones removed on operation or postmortem, but the first report of the roentgen demonstration of these translucent fissures in the living subject was by Breuer in 1931. A case is described in which three stellate central translucent shadows in the dye-filled gallbladder were the only sign of cholelithiasis. This is a rare sign. In the study of 655 consecutive cholecystograms the authors have found it in only one.

These central stellate fissures are usually filled with gas or fluid. When fluid is present there is no radiolucency as the specific gravity of the fluid is greater than that of the neighboring cholesterin. In this case the whole stone generally remains negative to roentgen rays but occasionally the fluid-filled central fissures are radiopaque. When the fissures are filled with gas or air the translucent star sign of Breuer may appear. When the stones dry after removal the fluid contained in them may be replaced by air. If there were gas in the fissures in vivo com-

monly it would seem that this stellate sign would be seen more frequently but possibly its demonstration is prevented by technical difficulties.—*Audrey G. Morgan.*

Joffe, Herman, and Wachowski, T. J. Relation of density of cholecystographic shadows of the gallbladder to the iodine content. *Radiology*, Jan., 1942, *38*, 43–46.

It has long been known that visualization of the gallbladder on the roentgenogram depends on a certain amount of iodine being contained in the bile. In order to determine the iodine concentration necessary for visualization the authors gave 4 grams of tetraiodophenolphthalein orally to 14 patients the day before cholecystectomy was performed. The next morning just before operation a cholecystogram was made. Operation was performed about an hour later so there could hardly have been any change in the iodine concentration of the bile in the interval. It was found that a concentration of 0.1 per cent gives a faintly discernible shadow but that about 0.29 per cent is necessary to give definite visualization and that above that concentration the density of the shadow increases with increase in the concentration of iodine.

To test the accuracy of this clinical impression experimental work was done with water phantom standards similar to those of Newell. Rubber bags 37 cm. in diameter were used containing 30 cc. of bile to which tetraiodophenolphthalein had been added with concentrations of iodine ranging from 0.14 to 0.93 per cent. These experiments, in agreement with the clinical work, showed that a concentration of approximately 0.25 per cent was necessary to give a faintly visible shadow on the cholecystogram. —*Audrey G. Morgan.*

Gordon, J. S., and Manning, J. J. An autopsy survey of gastro-duodenal ulcers in the Philadelphia General Hospital, 1920–1937. *Am. J. M. Sc.*, 1941, *202*, 423–432.

This article presents an analysis of the autopsies performed at the Philadelphia General Hospital for the seventeen year period from 1920 to 1937. The number of autopsies performed during this period was 22,956 and peptic ulcer was found in 548 of these cases, or 2.75 per cent.

Tables are given showing the incidence of peptic ulcer in different countries, their age, sex and race distribution, seasonal distribution, accompanying liver lesions and complications. There seems to be no true incidence of peptic ulcer which holds good at all times and in all places. Their incidence varies at different periods and in different locations. The figures for Philadelphia did not show any essential difference in the incidence in the white and colored races. There were about twice as many cases in males as in females.

There was a strikingly higher incidence of liver lesions in these ulcer cases than in the general hospital records. In spite of the variations in different countries and in different years peptic ulcer was quite constantly most frequent in the fifth and seventh decades of life.—*Audrey G. Morgan.*

Chont, L. K. Phytobezoar and its formation in vitro. *Radiology*, Jan., 1942, *38*, 14–21.

Nine cases of persimmon phytobezoar are described and illustrated with roentgenograms. A tabulation of the stomach findings in 26 cases shows that free hydrochloric acid was absent in only 2 cases. As this suggested that hydrochloric acid is a necessary factor in their formation the author made a study of the question of phytobezoar formation in vitro, using persimmons, prunes, raisins and celery in various solutions of decinormal hydrochloric acid with and without pepsin. Alkaline solutions of various strengths and water were used as controls. Bezoars were not formed in vitro by prunes, raisins, celery or completely ripe persimmons. Persimmons that were not completely ripe produced bezoars in any solution of hydrochloric acid with or without pepsin but not in alkaline solutions or in water.—*Audrey G. Morgan.*

Beling, C. Abbott, Baker, Charles F., and Marquis, W. James. Pancreatic calcification. *Radiology*, Feb., 1942, *38*, 188–190.

Lithiasis of the pancreas is very rare. Only about 142 cases have been reported in the literature and only 13 of these showed disseminated calcification. An examination of all roentgenograms of the intestinal tract made at St. Barnabas Hospital, Newark, N. J., from January 1, 1938, to January 1, 1941, showed only 1 case of disseminated calcification, which has been reported previously.

In this article an additional case in a man of forty-nine is reported. Ten years ago he was treated for an ulcer on the lesser curvature of

the stomach and was free of symptoms for seven years. The same symptoms then recurred and roentgen examination showed disseminated calcification of the pancreas. The man had been a heavy drinker of alcohol for many years. Under treatment he has improved, is able to do light work and is free of symptoms at times.

So little is known of this condition that all cases should be reported. Most gastrointestinal series are useless for this purpose for the pancreatic area is obscured by the shadow of the stomach or colon or flakes of barium remaining in the small intestine make differentiation of pancreatic calculi difficult or impossible. In making a gastrointestinal series therefore or a cholecystographic examination a flat plate of the abdomen should be made including the pancreatic area before the contrast medium is given. If any shadows are seen in the pancreatic area further examination is indicated. Lateral films are of value in showing the relation of the shadows to the spine. Stereoscopic films are helpful if there is calcification but they are not necessary unless other tests are inconclusive, such as amylase and lipase determinations and analysis of pancreatic secretion obtained through a duodenal tube, both with and without the use of secretion.—*Audrey G. Morgan.*

RITVO, MAX, and HEWES, FRED L. Clinical and roentgen manifestations of carcinoma of the duodenum. *Radiology*, Jan., 1942, *38*, 7–13.

Carcinoma of the duodenum is rare and until recent years no cases were reported that had been diagnosed during life. Only 3 cases have been seen during the past twelve years at the Pondville Hospital which has been functioning for that length of time under the Massachusetts Department of Public Health. This hospital treats only cases of malignancy and these cases of carcinoma of the duodenum constituted only 0.02 per cent of the total number of cases.

The cases are described. They were in males of sixty-four and eighty years of age and a female of seventy. The disease almost always occurs in old people and about two-thirds of the cases are in men. All of these patients died soon after admission to the hospital and diagnosis was made postmortem.

Neither clinical, roentgen or laboratory findings are characteristic in the early stages of the disease. As the tumor grows there is a change in the mucosal pattern with thickening or disappearance of the rugae. If the patient is thin and the duodenum can be compressed under fluoroscopic control these changes may appear quite early. Filling defects occur later and if there is localized ulceration flecks of barium may be retained in the ulcer crater. Few patients come for treatment early. In the late stages there may be narrowing of the duodenum, rigidity of the duodenal cap and decrease or absence of the normal markings.

Neither medical, surgical nor roentgen treatment is more than palliative. The average duration of life is six to eight months, the longest survival about two years.—*Audrey G. Morgan.*

RENDICH, R. A., POPPEL, M. H., and COVE, A. M. Roentgen diagnosis of space-occupying lesions in the region of the head of the pancreas. *Radiology*, Jan., 1942, *38*, 47–52.

The pancreas cannot be visualized directly by roentgen rays and cannot be made to absorb any radiopaque substance. Therefore changes in it can only be demonstrated indirectly by pressure effects. Enlargement of the head of the pancreas may be shown by protrusion into the gas-filled stomach or by various changes in the shadow of the duodenum. These changes are illustrated by roentgenograms. The duodenal loop may be enlarged or displaced to the right and anteriorly, the caliber of the lumen may be decreased, there may be changes in peristalsis and ironing out of the mucosal pattern, there may be a palpable mass and downward and forward displacement of the mid-transverse colon.

These changes, however, only show that there is an abnormal mass in the region of the head of the pancreas. The condition causing the enlargement may be a carcinoma, enlargement of the retroperitoneal lymph nodes, pancreatitis, other retroperitoneal tumors, such as sarcoma, cyst of the head of the pancreas, aneurysm of the anterior wall of the abdominal aorta or upward traction on the duodenum secondary to diaphragmatic herniation of the stomach. This is all that is shown by roentgen examination alone but by a careful study of associated clinical and laboratory findings it may be possible to make a more definite diagnosis.—*Audrey G. Morgan.*

MATTINGLY, D., and MENVILLE, L. J. Abdominal pregnancy. *Radiology*, Jan., 1942, *38*, 35–38.

Hysterography is of value in the diagnosis of both intrauterine and extrauterine pregnancy

but it may cause abortion. An effort has been made therefore to replace it by uterine soft tissue studies.

At the Charity Hospital in New Orleans there have been about 25,000 deliveries during the past five years, of which 10 (0.04 per cent) were cases of extrauterine pregnancy. Roentgen examination was made in only 7 of the cases and in 2 of these only flat films were made. The others were examined by soft tissue studies and hysterograms. A soft tissue study alone was made in only 1 case. A preoperative diagnosis confirmed by operation was made in all 5 cases. There were no abortions following hysterography in any of these cases.

In abdominal pregnancy the most important diagnostic signs are: absence of a uterine shadow if an opaque medium is not used, fetus high in the abdomen, transverse position of fetus, fetal parts just beneath the abdominal wall as shown by illustrative roentgenogram, fetal parts outside the uterus in hysterography.

All of the 10 cases reported here were in colored women. The maternal mortality was 40 per cent; all of the fetuses were stillborn except one, a normal, full-term infant delivered by operation.—*Audrey G. Morgan.*

GYNECOLOGY AND OBSTETRICS

Leventhal, Michael L., and Solomon, Ernest M. The therapeutic value of tubal patency tests in sterility and infertility. *Am. J. Obst. & Gynec.*, April, 1941, *41*, 628–640.

The patient complaining of sterility is seen on the date approximating the time of ovulation and she is instructed to have normal coitus just before the appointment. Carbon dioxide is insufflated transuterinely under low pressure and the tubes are declared impermeable to gas if no patency is demonstrated after three attempts up to 200 mm. Hg pressure. If the tubes are not patent to gas, the patient is instructed to report for lipiodol instillation within the following day or two. Serial roentgenograms are taken including a twenty-four or forty-eight hour film if no patency is shown initially. If lipiodol instillation fails to reveal any tubal patency, it is repeated in two months. In cases of tubal closure, the roentgenogram demonstrates the site of obstruction and is invaluable in checking cases suitable for surgical intervention.

In a series of 133 patients in whom the patency test could be evaluated, 54, or 40.6 per cent, became gravid. Twenty-eight, or 21.5 per cent, became pregnant within two months of the test, the pregnancy being attributable directly to the procedure. The authors feel that coitus immediately preceding insufflation probably added to the high percentage of successes and was attended by no ill effects.

In 6 instances where the tubes were patent to gas but non-patent to oil, pregnancy occurred only once. Thirteen of 20 patients who demonstrated no patency to gas and who later evidenced patency to lipiodol became gravid, whereas none of the patients who were negative to gas and on whom there was no follow-up with oil conceived. This observation may be interpreted as evidence for the superiority of lipiodol insufflation in the cure of sterility. The authors used lipiodol in 85 cases and noted the production of morbidity in only one patient who developed an acute exacerbation of an old pelvic inflammatory process. They believe that if contraindications are scrupulously observed, the use of lipiodol is attended by negligible morbidity.—*Mary Frances Vastine.*

Bray, Philip N. The fetal motion factor in the roentgenographic diagnosis of pregnancy. *Am. J. Obst. & Gynec.*, Jan., 1941, *41*, 113–117.

Failure to demonstrate fetal structures in the roentgenogram may be due to movement of the baby. In a case of the author's, an anteroposterior roentgenogram of the abdomen showed only one fetus while a lateral projection showed two. The anteroposterior view was then retaken and the two fetuses were seen. The literature on this subject was reviewed and the author found only one reference to complete obliteration of all fetal structures in the roentgenogram due to fetal movement. It is advised that in the endeavor to eliminate this error, (1) the lower bowel and bladder be empty at the time of examination, (2) both anteroposterior and lateral roentgenograms be taken, and (3) the exposure be not made until mother and fetus are quiet. The author suggests that the mother can usually tell if the fetus has moved during the exposure.—*Mary Frances Vastine.*

Morton, Daniel G., and Hayden, Charles T. A comparative study of male and female pelves in children with a consideration of the etiology of pelvic conformation. *Am. J. Obst. & Gynec.*, March, 1941, *41*, 485–495.

The pelves of 59 girls and 16 boys of ages varying from four to fifteen years were studied

roentgenologically in order to determine the pelvic shape from early childhood through adolescence and to compare the incidence of the various types with the incidence in adulthood. Three films were taken in each case to illustrate (1) the superior strait, (2) the lateral aspect of the pelvis, and (3) the subpubic angle. A modification of the Thom method was used.

1. The pelvic inlet was anthropoid in type in 71.2 per cent of the girls and in all of the boys. In another 10 per cent of the girls, while the pelves were not of the pure anthropoid type, marked anthropoid characteristics were observable.

2. On the whole, the pelvic inlet of both boys and girls of prepuberty age (under eleven years) was essentially anthropoid in type.

3. The pelves of the prepubertal children were indistinguishable with respect to sex except for a possible difference in the position of the greatest transverse diameter of the inlet (it seemed to be nearer the sacrum in the boys).

4. There were definite developments in the pelves in children of postpubertal age which distinguished them from those of the younger children. For example, the adult (including the postpubertal) anthropoid pelvis is an oval while that of the child does not present a smooth oval outline because there is an inward bulge in the regions of the acetabula. Marked differences between the pelves of the two sexes were noted in the postpubertal age. In the girls, there was a tendency to anteroposterior flattening so an increasing proportion of gynecoid pelves was found.

The authors suggest that both males and females start out life with pelves which are identical in type and that the major differences observed in adult male and female pelves do not appear until puberty and are therefore due to the influence of the sex hormones.—*Mary Frances Vastine.*

MISCELLANEOUS

Bach, Ernst. Zur Frage der Schädlichkeit der Röntgenstrahlen beim Röntgenpersonal und bei dem Patienten. (The question of injury to patients and personnel from roentgen rays.) *Strahlentherapie*, 1941, *69*, 95–120.

Experiments were performed on guinea pigs with the object of determining the amount of injury to be expected to patients and personnel from exposure to roentgen rays. As it has been claimed that roentgen irradiation decreases the resistance of the subject to infection, the irradiated animals were given diphtheria toxin after the irradiation. Some of the animals were kept in rooms where they were subjected for long periods to small doses of scattered radiation, as the personnel in a room for roentgen therapy would be.

Graphs are given showing the changes in temperature and blood picture from this treatment and descriptions are given of the changes found in the organs when the animals were killed.

The doses given were comparable to the therapeutic doses given to man, proportioned to the body weight irradiated. In considering the effects of irradiation the dosage per volume of tissue must be counted rather than the surface dosage.

The experiments showed that there is a general injury from roentgen irradiation which increases with increase in the volume of tissue irradiated and increase in the individual dose. Very small doses have a stimulating effect but with larger doses there is injury to the blood picture and decreased resistance to infection, which, however, is temporary. The body gradually recovers its original power of resistance.

The animals kept in a roentgen therapy room at first showed greater resistance than the control animals. But the mortality was greater at the end of two months than at the end of one and greater after three months than after two. So it is probable that considerable injury might result to personnel working for months or years in such rooms. When it is remembered that the function of the ovary can be completely abolished by a dose of 220 r the necessity for protection of roentgen personnel becomes evident. The official government regulations are that no one must work in a roentgen room for more than seven hours a day and not more than five days in the week. The free days should be spent as far as possible out of doors, and the roentgen worker must have at least a month's vacation each year.—*Audrey G. Morgan.*

Stenstrom, Wilhelm. Elimination of radioactive elements by patients and rabbits after injection of thorotrast. *Radiology*, Dec., 1941, *37*, 698–704.

When thorotrast is injected a series of radioactive elements are produced continuously from the thorium. A table of these elements with their half-value periods is given. Experiments

on 3 rabbits are described in which an attempt was made to determine the distribution of these radioactive elements in the tissues and their excretion. The technique of the experiments is described.

A table is given showing the radioactivity of the different organs of a rabbit killed 127 days after the injection of thorotrast. The activity of ash from liver, spleen and bone increased with time. The short period elements had evidently been partially eliminated during life. The amount of radioactivity per gram of material was 20 times greater in the spleen than in the liver and 4 times greater in the bone marrow than in the liver. There was very little in the shafts of the bones. The radioactivity in the blood and lymph nodes was evidently due chiefly to thorium X. Thorium X can be demonstrated in living animals by gamma-ray measurements but cannot be measured quantitatively.

The chief new point brought out in these experiments is that the different elements in the thorium series are distributed differently and are eliminated to a considerable extent from the tissues.

Excretion of thorium after intravenous injection of thorotrast has not been demonstrated in human subjects. The author reports 2 patients who had been given injections six and seven years before the measurements. The investigation showed that a great part of the thorium still remained in the tissues.

In the discussion Dr. Robert Taft said he did not believe that the information given by the injection of thorotrast justified the risk. Dr. Rigler said he was using thorotrast much less than he did eight years ago but he had no proof of any definite harm done by the injections. In closing, Dr. Stenstrom said that intravenous injection of thorotrast is a serious matter. He has used it as a sensitive method in order to determine whether thorium was excreted. So far he has not found thorium excreted but has found that some of the radioactive substances in the series are excreted, which decreases the amount of radiation, though of course there is still some radioactivity of the tissues.—*Audrey G. Morgan.*

Marinelli, L. D., and Kenney, J. M. The absorption of radiophosphorus in irradiated and non-irradiated mice. *Radiology*, Dec., 1941, *37*, 691–697.

Experiments are described which were made with the purpose of studying the effect of roentgen irradiation on the gross phosphorus metabolism of some animal tissues. Albino rats were used as experimental animals. Thirty-six animals were retained as controls and in the other 84 one leg was irradiated with 3,000 r in air, 190 kv. unfiltered roentgen rays, the exposure time being two minutes. The rest of the animal's body was protected with lead. Tracer doses of P^{32} were given intraperitoneally and the animals killed at varying intervals thereafter and the P^{32} content of the various tissues determined. Tables and graphs are given showing the details of the results. Irradiated bone was found to have a greater P^{32} content than non-irradiated bone. There was no significant difference in the amounts contained in muscle and skin. There was no difference in the P^{32} content of several non-irradiated tissues in the irradiated group and the control animals. When the concentration of P^{32} was studied with relation to time it was found that the rate of elimination of the substance by a given tissue is an important factor in the dosage of radiation given to the tissue.—*Audrey G. Morgan.*

Kenney, John M., Marinelli, L. D., and Woodard, Helen Q. Tracer studies with radioactive phosphorus in malignant neoplastic disease. *Radiology*, Dec., 1941, *37*. 683–690.

Small amounts of radioactive phosphorus (P^{32}) were given to patients with carcinoma of the breast, osteogenic sarcoma and lymphosarcoma. Small parts of the different tissues were removed surgically, reduced to ash and their radioactivity determined. The concentration of radioactive phosphorus in the given tissue, expressed in microcuries of P^{32} per kilogram of tissue was divided by the microcuries of P^{32} given per kilogram of body weight. The result was called the differential absorption ratio (D.A.R.) or the ratio between the amount of phosphorus absorbed by the tissue and the amount it would have absorbed if the phosphorus had been equally distributed throughout the body.

The object was to determine whether sufficient amounts of the radioactive substance could be localized in malignant tumors to be useful in the treatment of such tumors without damaging normal tissue. This paper does not discuss methods of administering radioactive

substances in malignant tumor. Such a discussion will be published in *Cancer Research*. But attention is called to the fact that large amounts of radioactive phosphorus may injure the blood-forming organs and seriously depress the blood count. Therefore a careful study of the bone marrow of the patient should be made before this method is used. Frequent blood counts and occasional marrow studies should be made during the treatment.

It was found that radioactive phosphorus may be a useful agent in the treatment of lymphosarcoma and a useful supplement to ordinary roentgen treatment in the other two forms of tumor studied.—*Audrey G. Morgan.*

Zahl, Paul A., and Cooper, Franklin S. Physical and biological considerations in the use of slow neutrons for cancer therapy. *Radiology*, Dec., 1941, *37*, 673–682.

The destructive action of roentgen rays and fast neutrons occurs throughout the tissue irradiated and there is no way of localizing it in the tumor zone. But as the passage of slow neutrons through tissue is not accompanied by the production of energetic recoil protons they do not injure tissue. But if the zone through which the slow neutrons pass has been perfused with certain chemicals, such as boron or lithium or their compounds, these materials capture the slow neutrons and reactions occur which release very energetic particles that destroy tissue. It should therefore be possible to produce strictly localized destructive action by slow neutrons by localizing the necessary chemical in the tumor zone.

Experimental work along this line is discussed. The most promising method seems to be the intravenous injection of azo and related dyes in which the sodium atoms have been replaced by lithium atoms. When such dyes were injected into tumor-bearing mice it was found that the concentration of lithium in the tumors was higher than in the surrounding tissues. The concentration in the tumor was high enough to indicate that irradiation with slow neutrons would result in a considerable difference in ionization between tumor and normal tissue, with resultant destruction of the tumor. The relation between the absolute concentration of the substances that capture neutrons and the difference in concentration in normal and tumor tissue is discussed. Before attempting to use this method clinically efforts should be made to increase the difference in concentration of the neutron-capturing substances in tumor tissue and normal tissues.—*Audrey G. Morgan.*

Goldfeder, Anna. Further studies on effects of irradiation on proliferation and metabolic processes of normal and malignant mammalian tissues. V. Effects produced by different dosage rates of x-radiation upon growth factors of mouse sarcoma 180 grown in vivo following irradiation in vitro. *Radiology*, Dec., 1941, *37*, 705–716.

The author has previously studied the effect of different doses of roentgen radiation on different animal tissues in vitro. In this article she considers the effect of different doses and time rates on the growth of mouse sarcoma 180 in vivo after irradiation in vitro. The fragments of tissue were inoculated into living mice within an hour after irradiation. Tables are given showing the details of the results. Filtered and unfiltered 200 kv. radiation was given with two time rates, one sixteen times as long as the other, the dosage being 40 r/min. in the one case and 640 r/min. in the other.

It was found that the critical doses were 2,000 and 2,200 r; that is, with a dose of 2,000 r only 1 tumor appeared seventeen days after implantation and with 2,200 r no tumors appeared. With these critical doses the effect was greater with the low dosage rate, that is with the longer time of administration which allowed time for the total destruction of a greater number of cells. The biological effects of irradiation depend on the dosage rate and time of exposure. A combination of proper dosage and proper rate of administration is necessary to bring about the desired results.

It is not known whether the results obtained in these experiments are applicable to spontaneous tumors.—*Audrey G. Morgan.*

Ellinger, Friedrich, and Gross, Reuben. Depth dosage measurements by means of goldfish. *Radiology*, Dec., 1941, *37*, 717–723.

The authors describe experiments made with goldfish used as biological test objects for roentgen irradiation. Goldfish were suspended in a dish at the top of a water phantom and also at varying depths in the water and the effect of different dosages determined as measured by the mortality of the goldfish. The goldfish were found to be suitable biological objects for this purpose.

It was found that with an increase in the dose measured ionometrically there was an increased depth effect but that with two unequal ionometrically measured doses the depth effect was not always proportionate, but might be greater than was to be expected from the ionometric measurement. Graphs are given showing the findings. Physical data should be checked by comparison with the findings in as many biological test objects as possible.

In the discussion Dr. Glasser said that Dr. Ellinger had used the mortality curves of the goldfish in studying effects, instead of the amount of radiation necessary to kill half the objects, which was the method used by Packard in studying *Drosophila* eggs. As the normal mortality rate of goldfish is rather high this might introduce an inaccuracy. Dr. Henshaw asked whether, in going from a lesser to a greater depth the sensitiveness of the biological object increased or whether the ionization chamber failed to detect some ionization that was effective biologically. The ionization measured in air may not correctly represent the ionization in the tissues. This does not discredit the use of goldfish for such studies. Dr. Ellinger replied that the very fact that ionization in air and in tissue may not run parallel made it necessary to study the biological action of roentgen radiation on as varied a material as possible.—*Audrey G. Morgan.*

Potter, J. Craig. The biological effect of roentgen rays of long and short wavelength on the totally irradiated rat. *Radiology*, Dec., 1941, *37*, 724–725.

This study was continued for eight years and 500 rats were totally irradiated, using heavily filtered rays at 400 kv., lightly filtered rays at 100 kv. and unfiltered rays at 100 kv. A table is given showing the results for the last 49 rats.

For filtered radiation the lethal entrance dose was 800 r at both 100 kv. and 400 kv. With unfiltered radiation the lethal entrance dose was 1,200 r. The exit lethal dose was the same for all the wave lengths studied. With all the wave lengths fertility continued up to the dose that caused death.—*Audrey G. Morgan.*

Chaoul, H., Schatter, T., and Wachsmann, F. Grandsätzliches über die Dosimetrie bei der Nahbestrahlung. (Fundamentals in dosimetry in close irradiation.) *Strahlentherapie*, 1941, *69*, 231–248.

The reports of dosage distribution with the Siemens close irradiation apparatus for Chaoul's treatment made by different authors vary considerably. Only the primary irradiation emitted by the tube is of value in treatment but in addition to this there is a secondary irradiation and an electrone irradiation, that is, photoelectrons emitted from the wall of the tube. These irradiations falsify the measurements made in the ordinary way.

A specially constructed chamber for making correct dose measurements is described and illustrated. It is called a sieve chamber as the essential feature of it is a grill made of silk threads covered with graphite stretched on a frame 1 mm. apart.

Curves for relative depth doses and isodose curves are given. Absolute accuracy in the measurement of close irradiation is impossible but in the close irradiation of superficial or exposed tumors the process of destruction of the tumor can be watched and the dose adapted to the individual case. The deep normal tissues are spared so that a moderate amount of overdosage does no harm.—*Audrey G. Morgan.*

Happey, Frank. The construction of a universal dosemeter with notes on its use for the measurement of high resistances. *Brit. J. Radiol.*, Oct., 1941, *14*, 336–340.

A universal dosemeter is described and illustrated. Its essential features are: (1) vacuum insulation of ionization current leads as far as possible; (2) a variable condenser system carried in a vacuum chamber and fitted with a "Townsend balance" circuit; (3) "air-walled" ionization chambers which are detachable and can be replaced by others of different wall thickness and size; (4) a series of high resistance from 70,000 to 1 000,000 ohms are carried in a rack outside the evacuated chamber; (5) the measuring instrument is a Lindemann electrometer mounted with a microscope.

The object in designing the instrument was to produce an apparatus capable of measuring ionization currents of widely different values, such as the radiation from a contact roentgen tube with an output of 10,000 r/min. or a radium applicator with an output of 50 r/hour. Diagrams of the instrument as a whole and of its parts are given. The method of continuous dosage measurement is described and directions given for the measurement of high resistances.

The instrument can be used for standardizing

either roentgen-ray or radium dosemeters, but for the former ionization chamber, walls about 1 mm. thick are required. If the material carbolite which is a mixture of graphite and bakelite, proves sufficient, "air-walled" chambers made from it can be used instead of those made from the German product "Aerion."—*Audrey G. Morgan.*

SCHÖNANDER, GEORG. A study of secondary screening. *Radiology*, Dec., 1941, *37*, 743–745.

The factors of importance in secondary screening are discussed. The author has made experiments which have established the height, width and distance between the strips of the grid which will provide a maximum of secondary screening with the least possible absorption and the least possible amount of shadow due to the strips themselves. That is to say the three factors of high Bucky effect, low absorption of primary radiation and absence of interfering shadows due to the diaphragm have been adapted as favorably as possible to one another.

Intermediate layers of aluminum, magnesium, beryllium and alloys with similar properties were tested. These brought about a reduction of the intensity of the radiation from the lead, as a result of absorption in the light metal intermediate layers. In order to eliminate the lead radiation altogether the lead strips were covered with a layer of tin which entirely absorbs radiation from this source. The strips of tin are covered with a nickel or iron layer and this, in turn, is united with the intermediate layer of light metal, which therefore needs only to absorb the soft radiation emanating from the nickel or iron.

The methods of measuring the Bucky effect, or secondary screening ability, are described. Estimating the Bucky effect by the primary darkening of the Potter-Bucky diaphragm gives 48 per cent Bucky effect and this new metal diaphragm 60 per cent. This gives increased contrast to the picture. Moreover the size of the strips and of the distance separating them are selected so that the shadows of the grid can scarcely be seen in the roentgenogram. The diaphragm can therefore be used without moving it. The grid is only about half as thick as the Lysholm grid and therefore the distance between the patient and the film is greatly decreased, which brings about increased sharpness of the picture.—*Audrey G. Morgan.*

STANFORD, BRIAN. A research into the physical factors concerned in indirect radiography. VI. The effect of varying the coating thickness of the fluorescing material of a screen on the luminous output obtained. *Brit. J. Radiol.*, Dec., 1941, *14*, 392–395.

The factors that influence the perfect performance of a fluorescent screen are discussed. Tests to determine the effect of the thickness of the coating on such output were made on two types of screens, G 231 and Y-S. The thicknesses used were 75 per cent, 100 per cent, 150 per cent and 200 per cent of the standard thickness. It was found that for screen G 231 a coating 75 per cent of the standard thickness is photographically more actinic than the standard thickness. For screen Y-S there was no gain in actinic output by using a thicker coating than the standard. Details of the findings are shown in tables and graphs.—*Audrey G. Morgan.*

HARVEY, ROGER A. A rapid dark adaptation test. *Radiology*, March, 1942, *38*, 353–354.

A method of determining dark adaptation time is described which can be used where an inexpensive and rapid test is necessary. An aluminum step tablet with 12 steps each 2.5 cm. wide, 10 cm. long and progressively increasing 1 mm. in thickness is placed on roentgen film. Lead numbers from 1 to 12 are placed on the steps and the film exposed. The degrees of density shown by the different steps are given. If an aluminum step tablet is not available strips of film can be arranged in order of increasing density. The film is placed against a fluoroscopic screen which is allowed to fluoresce only under the film area.

In testing a group of 14 doctors and medical students by this method the dark adaptation time was found to vary from three to twenty minutes. There are also variations in the same individual at different times of day. The strip of film described requires adaptation to strip 9 for chest fluoroscopy and to step 12 for gastrointestinal work for the installation used. The figures may vary slightly for other equipment. —*Audrey G. Morgan.*

BLONECK, FRANCIS. A universal table for the fluoroscopic localization of foreign bodies. *Radiology*, Feb., 1942, *38*, 174–185.

For military purposes rapid and easy methods of localizing foreign bodies are necessary

which are sufficiently accurate for purposes of war surgery and do not require special equipment. Such a method is described which can be adapted to any kind of horizontal fluoroscope. It is simple and rapid and does not require any computation or reading of scales in the fluoroscopic room. It requires the actual measurement of only two values: the thickness of the part containing the foreign body and the shift of the foreign body shadow on the fluoroscopic screen. The geometrical basis of the method is illustrated. It is based on the fluoroscopic application of the classical triangulation principle and can be used with a single or double tube-shift. A table has been worked out from which it is possible to determine the depth of a foreign body to within a fraction of a centimeter without calculation. Two nomographs which serve the same purpose are also given.—*Audrey G. Morgan.*

Corby, Robert A. A new method of localization by a modified use of the laminagraph. *Radiology*, Feb., 1942, *38*, 186–187.

A rapid, simple and practically automatic method of depth localization is described which is based on a modification of the laminagraphic principle. It has been used successfully for nearly three years and can be applied to any laminagraphic instrument that has a lever with an adjustable pivot or fulcrum connecting the roentgen tube and the Bucky or plate carrier. About the only necessary change in the apparatus is the addition of a scale to the roentgenographic table and a pointer to the plate carrier so that any change in the position of the carrier relative to the scale can be measured accurately.

The patient is placed on the table so that the tube is roughly over the expected position of the object when the tube and lever are in the perpendicular position. The pivot is raised to a position higher than that of the upper surface of the part that is being examined. An exposure is made just sufficient to penetrate the part. With the pivot at the same level the tube is moved an arbitrary distance in either direction, allowing the plate carrier to move to a new position. The apparatus is locked in place and a second exposure made on the same plate. The film is developed and the distance between the two shadows of the object on the film is measured with calipers. Then the pivot level is slowly depressed until the plate carrier is displaced a distance equal to the calipered measurement on the film. The pivot will then lie in the same plane as the object to be localized. The method is a means of forcing the two shadows to coincide, in this way causing the instrument to adjust itself correctly. A graphic demonstration of the geometric proof of the method is given.—*Audrey G. Morgan.*

Teperson, Hyman I. A simple film-drying shelf for the dark room. *Radiology*, April, 1942, *38*, 493–494.

A shelf for drying films in the dark room is described and illustrated. It is inexpensive and easily constructed and is tilted and provided with a rubber drainage tube. This prevents the untidiness which results, with the usual film-drying shelf, from the dripping of water on the floor.—*Audrey G. Morgan.*

Sussman, Marcy L., Steinberg, Morris F., and Grishman, Arthur. A rapid film changer for use in contrast angiocardiography. *Radiology*, Feb., 1942, *38*, 232–233.

A succession of rapid film images is of value in studying pathological conditions of the heart and great vessels. The two-film method has not proved adequate for physiologic studies and sufficient detail is not obtained with the fluorographic method. The authors describe a simple apparatus made to obtain a series of rapid exposures by direct roentgenography.

The apparatus is a wooden wheel 62 inches in diameter mounted on an axle. Eight 10×12 inch cassettes are mounted radially. The wheel is turned by hand behind a lead screen in which there is a 10×12 inch opening. An ordinary door stop is used to stop the wheel as each cassette moves into position behind the opening in the lead screen. With practice eight exposures can be made in ten seconds. This is a homemade type of apparatus and relatively inexpensive. It is described chiefly to stimulate further effort to produce a more perfect apparatus.—*Audrey G. Morgan.*

Erf, L. A. A note on the effect of dermal and enteral irradiation by radio-phosphorus on the blood levels of dogs. *Am. J. M. Sc.*, Nov., 1941, *202*, 650–654.

A hypertonic solution of radio-phosphorus was placed in rubber capsules, 2.5 cc. to a capsule, emitting 5.5 millicuries of beta radiation.

The capsules were fed to dogs in some cases and applied to the skin in others.

The blood counts of the dogs treated by the two methods are given and a graph showing the trends of the absolute numbers of circulating lymphocytes before, during and after dermal and enteral irradiation with radio-phosphorus. There were no significant changes in red cell and platelet counts or hemoglobin levels. In cases in which the rays were applied to the skin there was a slight decrease in the absolute number of lymphocytes. In the cases in which the radio-phosphorus was given by mouth there were significant changes in the absolute number of lymphocytes, evidently caused by the action of the radio-phosphorus on the lymph follicles of the intestine. These follicles are quite frequently hyperplastic in patients with lymphatic leukemia, less frequently so in those with myeloid leukemia.

These experiments suggest that it may be possible to give irradiation by mouth to patients with these diseases.—*Audrey G. Morgan.*

Janzen, Arnold H., and Warren, Shields. Effect of roentgen rays on the peripheral nerve of the rat. *Radiology*, March, 1942, *38*, 333–337.

It is important to know the effect of irradiation on the peripheral nerves as they are constantly being exposed to increasing doses. Experiments were therefore made on rats in which the sciatic nerves were exposed and the right one exposed to varying doses of 4,000, 6,000 and 10,000 r generated at 200 kv., while the other one was used as a control. The animals were killed after intervals of from twenty-four hours to eight weeks and histological examination of the nerves made. Photomicrographs of the findings are given. During life the animals did not show any bad effects from the irradiation and there were no histological changes that could be attributed to it.

When the nerves were exposed to 1,200 to 1,600 millicurie-hours of radium irradiation there was complete degeneration of the nerve and some signs of degeneration of the sensory neurones.

The experiments show that nerve tissue is extremely resistant to irradiation.—*Audrey G. Morgan.*

Evans, T. C., Goodrich, J. P., and Slaughter, J. C. Temperature and radiosensitivity of skin of new-born rats. *Radiology*, Feb., 1942, *38*, 201–206.

Experiments were made on newborn rats to determine whether the degree of injury by roentgen rays could be affected by controlling the metabolic rate of the cells. It was first found that the resistance of the skin of the rats to irradiation was greatly increased by chilling them to near 0° C. during irradiation. To see whether this was due to the lowering of the metabolic rate caused by the cold, other methods of lowering the rate of metabolism were tried, such as taping the animals so that they could not breathe for fifteen to twenty minutes and ligating the vessels supplying a part and then irradiating.

The exposure time in all the experiments was fifteen minutes and the dose 2,010 roentgens. The target distance was 30 cm. The radiation was unfiltered except for 2 mm. cardboard and the half-value layer was about 1.5 mm. aluminum.

All of these methods of lowering the metabolic rate increased the resistance of the skin to irradiation. The experiments offer some hope that it may be possible to increase the therapeutic action of roentgen rays by changing the ratio between the tolerance of normal tissue and that of tumor tissue.—*Audrey G. Morgan.*